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EDITORIAL.

STUDY AND EXAMINATIONS.

Once more as the days roll by and the end of the term draws near, we hear the old cry, "Time to start working for the examinations."

We would like to suggest that a great many undergraduate students of medicine are working for the examiners rather than for themselves. The passing of examinations is of prime importance, and the accumulation of knowledge, which will be the basis of their practice of medicine, is a secondary consideration.

It is true that this attitude is fostered by the educational system—a system which spoonfeeds from the start. Unfortunately, the classes are so large that it is difficult to form an opinion of the ability of the individual. The examination forms the chief source of this information.

So, until this system is changed we must make the best of it. We must get out of the rut. We can do this only by changing our outlook; by forgetting the bugbear of examinations. Study for the sake of learning and the examinations will take care of themselves.

"Take therefore no thought for the morrow: for the morrow will take thought for the things of itself."

Consider the subject of lectures. We well know that, in many courses, we need only learn what is contained in the lecture notes to answer any question on the examination paper. But, are we to be content with this? It does not take a genius to memorize a set of notes and remember long enough to transfer the appropriate portions to the examination book. Lectures should be merely a guide to our study, pointing out to us those parts of the subject which are more important.

Moreover, our teachers are only human beings. We must consider their views with an open mind, consulting text books and journals for the views of others and, if possible, experimenting for ourselves. We draw our own conclusions, deciding in our own minds what solution is the most logical. When we graduate we may not have others to think for us.

But we, too, are only human beings. There will be many times when the printed page will become blurred after weary hours of study. We set aside these weighty volumes of present knowledge and seek a stimulus to further effort.

We may, perhaps, pick up a book which tells of the lives of great students of the past, of how they labored to solve the mysteries which to-day are commonplace. We read of the untiring industry and self-sacrifice of these men and consider with what little expenditure of energy we may make their knowledge ours. Then, we may return to those heavier volumes with renewed energy and interest.

This, in our opinion, is the chief value of our journal—to stimulate interest in the study of medicine. So, as the examinations draw near, remember that they are incidental. We do not learn to drive an automobile in order to obtain a driver's license.

Few are called upon to abuse their memories more than the medical student; examinations demand a real amount of memory strain. At the same time we should realize that if from our earliest student days we could train ourselves to think more, we should be saved hours of tedious cramming.

Some of us hardly stop to think at all—in fact our curriculum allows us little time to do so. We try to remember innumerable signs and symptoms —diagnostic tags, etc. Some of this is necessary, but a deal of trouble would be saved, if we made ourselves form certain good habits. For instance, the careful routine examination. This is no strain on the memory, once the habit is established. It should become pure habit, to examine the urine, the pupils, the chest, the back, the hernial orifices and so forth, whenever the abdominal case comes under investigation. By so doing we shall frequently prevent the opening of a normal abdomen. Again, it has been truly said that sooner or later, if you fail to put your fingers in the rectum, you will put your foot in it! Most of the mistakes we make will be due to incomplete investigation, rather than to lack of actual knowledge.

We might with advantage cultivate the habit of regarding all cases as "interesting." The "chronic appendix" may turn out to be a spinal tumour; backache may be due to a carcinomatous metastasis in a vertebra. In the number of cases in Hospital, it is the recognized thing to get interested, and perhaps excited, over some rare and unusual condition. We must remember, however, that the good doctor is he or she who knows how to treat well the ordinary conditions—the little things: the whitlows, the piles, and other minor complaints.

Finally, we must train our minds to appreciate the early evidences of more serious disease.

By R. V. Cooke, in "The Leech."

With a great deal of pleasure we noted in the October number of "The Diplomate" the reprinting of an article published originally in the March, 1930, number of our Journal. This article, entitled "The Oldest Surgical Treatise," was written by Mr. O. E. A. Stephens, 3T4, whose article on "The History of Diabetes" appears in the present number.

We consider it a matter of pride to the Journal and of congratulation for Mr. Stephens that the National Board of Medical Examiners of the United States should think so highly of this contribution as to reprint it in their official publication.

An Eighty-Year-Old Valedictory.

[We are indebted to Dr. E. Stanley Ryerson for a copy of this address, which was delivered on March 1, 1851, to the graduating class of the Philadelphia College of Medicine, by Dr. Frederick A. Fickardt, Professor of Obstetrics and Diseases of Women and Children. There are surprisingly few respects in which this address is not applicable at present. The warning as to alcoholic addiction was probably more needed 80 years ago than today. In view of a recent tempest in a teapot, the reference to atheism is interesting. The advice on sending bills is obviously addressed to a more lesurely age than ours.]

It is a saying, gentlemen, with our countrymen, that "the price of Liberty is eternal viligance." The price of Knowledge is eternal thought; and to acquire Knowledge *is now your sacred* duty. Do some of you say—Have we not graduated? Ah! gentlemen, that graduation, honorable as it is to you, and much labor as it has cost you, is but the first fair step upon your path. Let none deceive themselves. Your weightiest study has just begun. You have learned the elements with us, but *with yourselves* lies their wide and various application and extension. We have given you the key-facts, but their vast and wondrous, their mysterious and solemn chambers you must explore alone. In your libraries, at the side of the sick, the suffering and the dying, alone, at all times of day and night, you must arrange, combine and apply them; and still by faithful study multiply your vital store.

Oh! what a labor? Oh! what a glorious privilege and power! How sublime to heal the sick, the lame, the blind, the deaf; to still the aching brain; to soothe the throbbing heart; to banish burning fever; to stay disease; to stand by the bedside of the father, the mother, the husband, the wife, or the child, and arrest the very uplifted hand of Death! Oh! this is noble, *and worth the double of your toil!* Who then will not labor for it? Who, to achieve this magnificent benevolence, this grand capacity in Medicine, will not diligently read, study and reflect, and sift and weigh and judge?

Press on then, Graduates; time past, time present, and to come, are open before you. Seize on their revelations with eager hands and complete the work you have so worthily commenced. Let nothing discourage you. As you advance on your way brighter scenes and greater facilities will open upon you; the rugged road will become smooth, and all its Alps subside before your growing and mightier knowledge. Be bravely aware of your position and your powers. Gird up your loins—summon up your courage—bend all your energies to the task and resolve to conquer.

Success, gentlemen, demands the cultivation of your intellectual faculties. How? By one great overshadowing Rule: *Think for yourselves.* Read, hear, gather opinions, but *think* for yourselves. Swear by the words of no man. It is our own thought which develops the higher reflective and creative powers of the soul, and makes the passive memory vigorous by its deep impressions. It is our thought only which gives us a true substantive and independent property in general or particular Science. All other knowledge is factitious; a borrowed stock in trade, a superficial prosperity of intellectual possession, fugitive in character and unreliable in crises. But a beautful or important thought won from the hard soil of facts by "the sweat of our brows," is our own; and being logically possessed in all its parts, becomes a living idea, endowed with our own spirit life, and available to every purpose of its knowledge. In such thoughts men have faith; —for such they toil;—with such they achieve their triumphs; and through such their memories become immortal. Genius is god-like, talent is admirable.

wealth gives facilities, and refined education is excellent, but neither the one nor the other can supply the place of *your own thought and your own industry*. Remember then, gentlemen, that you hold in your own hands your own destinies.

With regard to Theories and Systems let nothing sway you to the surrender of your own judgments. Do not fall into the common weakness of supposing one System perfect and all others *totally false*. You will learn, as you grow more experienced, that each has truths and untruths, merits and demerits, although not, perhaps, in equal ratio. *Acquaint yourselves with all*, and thus perfect your knowledge, and extend your catholicity of truth. You are the honorable Graduates of the oldest and best Systems of Medicine in our view. But shall you on that account close your eyes to all other systems? Will you exclude yourselves and your patients from the benefits of all other reaches of remedial experience and thought? I am persuaded you will not. Search, gentlemen, for facts, and discarding the tyranny of theories, variable as the wind, embrace the truth wherever you find it. Thus free you will reap a harvest of golden ideas. Your Practice will be comprehensive, pleasant and curative, and yourselves truly "Doctors," or *learned*, in Medicine.

Next, gentlemen, a high morality is essential to give full effect to your attainments. Integrity is the basis of all lasting reputation and usefulness, and commands alike the confidence and respect of friends and foes. "Do as you would be done by," is the great and controlling rule. This covers all morality—all honesty—all love—all duty—all truth; and not only satisfies Earth but applies itself to Heaven. Observe the pure teachings of this rule, and your reputations will brighten in the eyes of men; your influence will be enhanced, and your studies and Profession illustrated.

Let me point out to you, however, one snare which may entangle your feet unawares; a pit into which many of the Profession fall—yet not more than others. I allude to the treacherous habit of the use of stimulant drinks. The severities, the irregularity, the trials and exhaustions, the cold, the wet, the hunger, the travel by night, and the sleepless vigils of Medical life, present but too many and strong temptations to receive the temporary support of Alcohols. The hospitality of the people, too, increases the evil—misjudging friends, who thus drug the bowl of life with sorrow, shame and death! It has been my sad experience to behold many of my early medical acquaintances thus cut off in the flower of their lives, in the midst of their usefulness, and more than once, in the full view of the most cheering prospects. I cannot easily comprehend how Medical men shall permit usage of this sort to blind them to its dangerous tendencies, and the piosonous character of their draughts. The systemic unfitness of Alcholic liquors; their everywhere rejected presence in the economy; their irritant and excitant actions; the injurious states of the brain and abdominal viscera they induce; the serious organic lesions, and additional risks of recovery from sickness or accidents attached to their frequent imbibition, are so many daily evidences of the impropriety of their use.

It amazes me, gentlemen, to hear it charged that the Profession is *Atheistical*.

In the concise language of an able demonstrator of Anatomy "the Anatomist who is an Atheist *is a fool*."

No man may warily scan the coursing arteries, the returning veins, the intelligent nerves, the receiving and forcive heart, the vivifying lungs, the crowning brain, the thousand surprising arranements of bones, and muscles, and tendons, and pulleys, the precise and wonderful adaptive action of parts, direct and indirect, the miraculous conformation of those subtle organs whereby we receive the rays of light, the vibrations of sound, impressions of odors, taste and

touch, and yet refuse his solemn assent to a *Great Intelligent First Cause.*

As to the Rank of your Profession, assume that it is equal to any Arrogating to yourselves nothing that is offensive to others, permit nothing offensive from them.

In deeds of wide and fraternal humanity, in devotion to the sick and suffering; in that *true heroism,* braver than the soldier's, that faces death without glory: that unattended, encounters the plague, the cholera, the small-pox and a multitude of loathsome and infectious diseases, the Profession wears a crown of laurels forever green.

In your intercourse with the community take a right position and maintain it. The respect of the world is desirable, and important to you. The world respects those *who respect themselves, and those only.* "Make no enemy nor lose a friend." Nothing is more variable and extraordinary than the revolutions of a life-time. So singularly are the affairs of men blended together, that none knows at what point, or at what moment, he may need the good offices of another, or have reason to regret his hostility. Such is human life and the changeable current of its events, that the despised and injured individual of today is often the strong and powerful men of to-morrow. The truth strikes all observant men as they review the drama of life; and more than one, professional and lay, has bitterly repented the anger, the scorn or unkindness of irrevocable days.

Toward your Professional Brethren be affable and frank. Sacredly adhere to the etiquette established among Physicians for the preservation of Professional harmony and good feeling. Let nothing induce you to forget the dignity of your calling in unworthy efforts; or in remarks derogatory to the merits of those in competition with you. To hope, as some do, to build up a reputation on the defamation of a rival, is one of the most preposterous propositions with which the Medical heart ever deceived itself. That man only can erect to himself a solid and useful reputation, who to scientific attainments unites industry and of strict integrity of general and Professional conduct.

To the Profession and to humanity, gentlemen, you owe it, to be careful as to the qualifications of those you receive into instruction. Accept none whose mental powers and attainments are unequal to the Profession; nor any whose principles are opposed to its honor. As the homes of the Country are chiefly the sources of its social and moral principles, so are the Medical offices responsible for the men who issue from them.

In the choice of your Medical armament receive only the most approved and best medicines and of the purest sort. Refuse all cheap and doubtful drugs. In nothing is it more important to have reliable agents than in the sick-room, when perhaps a life hangs trembling on the efficacy of a single dose. With regard to the number of your medicines a proper understanding and control of established good remedies, will better promote your successful treatment than a too miscellaneous and multitudinous resort. A skillful artisan needs not many tools.

Let your Diagnosis of disease be careful and comprehensive. In your medication be closely attentive to all circumstances of constitution, temperament, habits of life, mental and physical, idiosyncrasies, hereditary tendencies, age and sex.

In the Practice of Medicine learn to look conditions promptly into shape, and form to yourselves at an early moment, clear and definite ideas of the disease you encounter. To do this accustom yourselves to take in quickly all essential symptoms of cases, and as readily to reject those not special, or merely associate.

Be sparing of Prognosis. Disease varies as the changes of the day. In serious cases be neither arrogant nor despondent, but watchful and attentive, and ever as *cheerful* as circumstances will admit. Endeavor to inspire your patients and those around you with con-

fidence so far as is just. The words, the tones, the looks and conduct of Physicians are often as potent as their remedies. When occasion requires, be unwearied in the application of your best skill; and in dangerous contingencies refuse to yield your patients until beyond all reasonable hope. None can infallibly tell when the dread fiat has gone forth from the Throne of the Almighty; or when it may be happily stayed. Often at the verge of life, when Nature's tide apparently stands still—at its lowest ebb—never to know reflux more—the ruby stream of being recommences a healthful flow, and the father, or the mother, the child, the sister, or the brother, the husband or the wife, already mourned as dead, is borne back to life, and home, and friends, and happiness again.

To the *poor be kind,* and to their Medical wants assiduous. They sufficiently need sympathy and aid when sick. Look upon them as children of the Great *Father* who is in Heaven, and you will not fail of your reward.

In the field of Surgery be prudent, rather than bold and fearless. Do not rush recklessly at every opposing obstacle, knife in hand. The scalpel is the last resort of the truly scientific Surgeon; and is, not unfrequently, a tacit admission, either of the deficiency of the operator, or the inefficiency of the healing art. It is now universally agreed in the Profession, that steel-edged Surgery should be far more sparingly employed than formerly. Surgery is indeed a noble art—requiring various and precise knowledge, great discriminative powers, calm courage, and unwavering steadiness of mind and nerve. Thus mentally and physically accomplished, the Surgeon occupies a proud position; nor can I commend to you a better exemplar than your own able and popular Professor.

In that delicate and important department which relates to the gentler sex, let a generous courtesy and the most scrupulous honor and purity continually attest the esteem in which you hold woman, and the respect which is so eminently her due. Woman, tender, and physically weaker than man, yet supports the most painful and heaviest part of the burden of life. In all the affections she is our superior. She is God's smile upon the Earth. As mother, sister, daughter, wife, or lover, *we* cannot match her qualities. Without her essential traits, man would relapse into barbarism, and human nature *shrink* beneath a wintry and perpetual frown.

In the general pursuit of your Profession *fix your aim.* In this and *perseverance* lies the secret of success. Men who climb a mountain toil. Those who view the ascent and dream of Aladdin's Lamp, or the ring of the Genius, *may dream,* but when they *awake* they will find themselves at the bottom. The law of success in science is labor; and it is by the *use* of talents, not their possession, we *rise* in life.

Do not diverge from the upward path. When some seemingly beautiful light shall dazzle you with its glare and fascination, some deceit of partisan politics, some meritricious lure of sudden wealth, or any other anti-professional temptation, turn from it as an ignis fatuus that will mislead and lose you. Fix your sight on your pole star and press on.

Never procrastinate. "Time is the stuff life is made of." An hour may be life or death to the patient: nor can you know in what direction the energies of practice may demand your presence in the next. "Tomorrow is nowhere but in the fool's calendar," and ceases daily to thousands.

It is the just employment of time and by judicious concentration of effort that great results are generally obtained.

"How," said a gentleman to another, celebrated for his vast labors, "do you accomplish so much—have you any plan?" "I have," was the reply, "when I have anything particular to do *I go and do it.*"

"How,' said another, to one of our most eminent statesmen, "do you manage to do so many things?" He replied, "By thinking of one thing at a time.'

In your money affairs be systematic

and correct. Many excellent men fail of their mark by neglect of this point. Be prompt in your collections. "Short accounts make long friends," and nothing more frequently and unpleasantly disturbs Physicians and families than an unwise postponement of settlements. Parties are prone to forget the many and important services rendered, and naturally take exception at amounts, which on earlier presentation, or with less accumulation, would have been held moderate and cheerfully liquidated. It is but just to families, and to yourselves to present your bills semi-annually.

Exercise economy in the expenditures of your early years. Look forward to the attainment of a proper and comfortable independence, before you shall have passed the prime of life. Every Medical man should at forty years be reasonably independent, under common circumstances of Practice. Beyond independence do not care too greatly for wealth.

It is a mistake to suppose *happiness can be purchased.* Above that honorable and useful measure I have indicated, it is a question with well balanced and experienced minds whether riches are desirable. The private history of Astor, Girard, and McDonough does not indicate great value in possession.

Knowledge, wisdom and virtue, gentlemen, are worthier than wealth. They are fuller of fruition; they approximate man nearer to God. And what shall interject itself as a barrier to the mighty and resolute will?—what limit the knowledge of the earnest Soul? Not anything, gentlemen! Little by little, steadily and with method, braced by thought and patient industry, temperance, integrity and reliance on Almighty God, move on and win the eminence of your Profession.

Cyanosis.

By J. HEPBURN, M.B.

Cyanosis is the grey, blue or even purplish colour of the skin and mocous membranes, commonly seen in sufferers from cardiac and respiratory diseases, but occurring more rarely in other conditions.

Our present knowledge of cyanosis dates back only a dozen years and is due to the work of Lundsgaard, who ferreted the truth from a perfect warren of unproven theories and conjectures.

CO_2 theory.—One of the most popular theories was (and still is even in current textbooks) that cyanosis was due to an excessive amount of CO_2 in the blood. This view is only mentioned to be condemned as it is most improbable that acidosis alone can on the one hand prevent the oxygenation of the blood in the lungs and on the other hand increase the dissociation of oxyhaemoglobin in the tissue capillaries, to an extent sufficient to cause cyanosis.

Methaemoglobinaemia and sulphaemoglobinaemia.—Another of the views that held sway before Lundsgaard, was that methaemoglobinaemia was the cause of cyanosis. Excessive consumption of certain drugs, *e.g.*, nitrites, potassium chlorate, acetanilide, etc., may lead to cyanosis. These abnormal haemoglobin compounds can readily be detected spectroscopically.

There is a very small group of cases of methaemoglobinaemia and sulphhaemoglobinaemia, occurring mainly in women with a history of constipation or diarrhoea or both. This form has been called enterogenous cyanosis and round it a battle of theories is still being waged. A nitrite-producing bacillus is said to have been isolated from various secretions, but unfortunately for the sup-

porters of this view, the bacillus does not live at body temperature.

One cure is reported in the case of a woman with enterogenous cyanosis which cleared up when a rectal stricture was relieved, and in a case at the Toronto General Hospital a left lumbar sympathectomy cleared up the cyanosis.

These cases due to drugs and intestinal absorption from a very small proportion of cases of cyanosis, and I have purposely dealt with them first, before going on to discuss the cause and mechanism of cyanosis as commonly seen clinically.

Common Causes of Cyanosis.—An understanding of what is meant by the terms, oxygen saturation, and oxygen content of blood (expressed as volume per cent) and the relationship of these two terms to one another, is absolutely essential for a clear comprehension of cyanosis.

Blood exposed in a thin film to an atmosphere of pure oxygen is fully saturated with oxygen, *i.e.*, its percentage saturation is 100 per cent; whereas blood exposed to alveolar air is 95 per cent. saturated with oxygen, all of which is combined with haemoglobin, except about 0.36 c.c. per 100 c.c. of blood, in solution.

The oxygen content of normal arterial blood is about 20 c.c. per 100 c.c. of blood, *i.e.*, the oxygen content of arterial blood is normally 20 volumes per cent.

The per cent. saturation and the volumes per cent. usually vary together, but this is not necessarily so, *e.g.*, the arterial blood of an anaemic person with 50 per cent. haemoglobin picks up in the lungs 95 per cent. of the oxygen it can carry, but the oxygen content is only 50/100 of 20, *viz.*, 10 vol. per cent.

A further illustration may suffice—the arterial blood of a patient with polycythaemia (*e.g.*, 200 per cent. haemoglobin) is again 95 per cent. saturated with oxygen, but the oxygen content is 200/100 of 20, *viz.*, 40 vol. per cent.

Lundsgaard has shown that cyanosis only occurs when the capillary unsaturation is greater than 6.7 vol. per cent. (more correctly, instead of capillary unsaturation, the term should be unsaturation in the subpapillary venous plexuses). As 1 gram of haemoglobin carries 1.34 c.c. of oxygen, cyanosis occurs when the subpapillary venous blood contains more than 5 grams of reduced or unoxygenated haemoglobin per 100 c.c. of blood. The point to be stressed is that the figure 6.7 vol. per cent. is absolute and not relative, *i.e.*, it does not matter if the patient's arterial blood can carry 7 c.c. or 40. cc. of O_2 per 100cc., that patient will be cyanosed in either case if the venous unsaturation is greater than 6.7 vol. per cent.

There are two main causes of cyanosis —faulty aeration in the lungs and excessive loss of O_2 in the tissues.

In many clinical cases both these causes are at work in the same individual.

Faulty Aeration or the anoic cause. —A few illustrations should serve to indicate how the blood may leave the lungs only partly saturated with oxygen—*e.g.*, dwellers at high altitudes—people with obstructions in the respiratory passages—more commonly seen are the cases of bronchopneumonia with the alveolar spaces partly filled with exudate, and the respiratory movements often made shallow in an attempt to lessen the pain of an accompanying pleurisy. Here two factors are at work, namely, shallow breathing which Haldane showed will produce cyanosis in a healthy person because of the poor ventilation of the lungs. The other factor is the mechanical obstruction to diffusion of O_2 through the pneumonic exudate.

Excessive loss of O_2 in the tissues or stagnant cyanosis.—Theoretically, greatly increased muscular work should cause cyanosis by its excessive call for oxygen, but this is looked after by increased blood flow.

The loss of O_2 in the tissue capillaries, leading to cyanosis, is usually due to marked slowing of the circulation, such as is seen in exposure to cold and clinically in cases of heart disease.

Usually in heart disease there is also

defective aeration, because of poor pulmonary circulation leading to thickened congested alveolar membranes often with transudations of fluid into the alveolar spaces, and at times with more or less extensive pleural effusions which further decrease the aerating powers of the lungs.

Cyanosis may also be due to the presence in the arterial system of venous blood which has not passed through the lungs as in some forms of congenital heart disease.

The foregoing account refers to general cyanosis, but cyanosis may also occur locally in any part of the body and is due to local stagnation of blood which is usually due to venous obstruction.

While Lundsgaard has cleared up the situation to a large extent, there are still unsolved problems, *e.g.*, why is cyanosis of the lips so common in heart disease and so uncommon in cases of pneumonia with marked cyanosis elsewhere?

Certain apparent paradoxes crop up in the study of cyanosis:

(1) In the forced breathing experiments conducted in physiological laboratories, why do some of the students become cyanosed while they are overbreathing?

The answer probably is that the alkalosis resulting from washing out of CO_2, causes peripheral vascular dilatation, fall of blood pressure, and peripheral stagnation of blood.

(2) Why does a case of severe anaemia not become cyanosed under any condition?

Because such a patient has not enough haemoglobin to give a venous unsaturation of more than 6.7 vol. per cent., *e.g.*, a patient with 30 per cent. haemoglobin can only have an unsaturation of 6 vol. per cent.—30/100 of 20 equals 6 v. per cent.

(3) Why does a marked case of polycythaemia, even with an oxygen-carrying power of 40 volumes per cent. become readily cyanosed?

Because the greatly increased number of red blood cells causes increased friction and consequently slowing of blood flow in the smaller vessels.

The Nausea and Vomiting of Pregnancy.

By P. G. SHUMAN, 3T1.

The nausea and vomiting of pregnancy was first described by Soranius in the early part of the first century. To-day these symptoms are recognized as manifestations of one of a group of disorders of metabolism which are directly due to the pregnancy itself. These disorders are known as the toxemias of pregnancy, and of these nausea and vomiting is by far the most common since it occurs in about every other pregnancy.

In its ordinary form nausea and vomiting usually appears at about the sixth week of pregnancy and disappears spontaneously about six weeks later. This so well known "Morning Sickness" is, in the great majority of cases, attended by no more serious consequences than the actual discomfort connected with it. For this reason it is often regarded as a more or less physiological process.

In some women, however, the ordinary "Morning Sickness" assumes a much more serious form, becoming characterized by the very distressing state of more or less continuous vomiting. It then becomes known as Hyperemesis Gravidarum, or the pernicious vomiting of pregnancy. Williams cites the incidence of this graver condition as once in a hundred and fifty pregnancies. Hyperemesis gravidarum is then much more common than is eclampsia and as all cases are preceded

by the ordinary nausea and vomiting it must be conceded that the condition is largely preventable. The prevention of pernicious vomiting would appear to depend on the acceptance of the view of many investigators that the ordinary Morning Sickness is always pathological from its inception, and that it is in this early stage that treatment must be instituted to forestall a possible hyperemesis.

Nature of the Toxemia.

It is not the intention of this paper to attempt to outline all the theories which have been advanced as to the cause of this disease. Toxemias of pregnancy must all still be characterized as diseases of theory for the reason that despite intensive work along various lines their origin is as yet entirely unknown.

Many of the older theories have been mere unsupported suggestions, and most of these must now be abandoned. There are several, however, which must still be considered because of the popularity which they have enjoyed, and because they indicate the lines along which recent investigators have worked rather than as affording any satisfactory explantion of the cause of the disease. These are the absorption theories, the endocrine theories and the carbohydrate deficiency theories.

Absorption Theories.

That the toxemias of pregnancy were the result of absorption into the maternal circulation of some product of gestation forms the basis of many theories regarding these conditions. Bourne contends that a toxin is constantly being produced by the growing ovum but that in all healthy mothers most of the toxin is effectively counteracted by their own immunizing efforts. Numerous observers have obtained toxic results by injecting placental extracts into animals and have postulated an unidentified toxin from the placenta as the primary causal factor in Nausea and Vomiting. Other popular theories have been based on absorption of waste from the foetus. There is little evidence of this, however, and it is unlikely that the end products of foetal metabolism differ in kind or toxicity from those of the maternal body. That the toxin is specific from the foetus is hardly likely in view of the well authenticated cases of pernicious vomiting occurring in the presence of hydatidiform mole.

Apart from the source of these hypothetical toxins much ingenuity is seen in theories of the nature of these toxins. Schmell has shown that foetal protoplasm is conveyed into the maternal circulation by demonstrating small pieces of syncytial protoplasm in the maternal circulation. Various theories then rest on the assumption that the protein of the foetus and its appendages behave as foreign proteins in the maternal organism. With these theories may be placed the opinion of other workers that the source of the toxin is the intestinal tract of the mother, first advanced by Dirmoser in 1903.

In reviewing these various suggestions it can only be said that no one has ever satisfactorily demonstrated the presence or source of any toxic body, been able to isolate such toxin or develop an antitoxin. The evidence is not convincing and most workers find it difficult to see how the supposed toxic agent could produce the lesions and symptoms known to be present.

Endocrine Theories.

The tremendous interest which resulted from the study of the effects of the ductless glands on metabolism and their connection with the sexual glands naturally led to investigation of their effects on the pregnant state. As a result the various endocrine glands, one after the other, have been accused of being the primary causal factor in the toxemias of pregnancy. The thyroid, pituitary and suprarenals

were in turn implicated and splendid results claimed from the use of their extracts. Silvestri, Sergent and Rathey quoted by Stander believe that in insufficiency of the adrenal gland and polyglandular activity one may discover the cause of the vomiting of pregnancy. Sella considers insufficiency of the ovarian secretion the causal factor.

Since 1916 the most prominent theory has been that of Hirst who believes that the corpus luteum plays an important part in the etiology of this condition. He argues that every woman during her menstrual life is constantly absorbing corpus luteum substance but with the onset of pregnancy this absorption ceases. The corpus luteum of pregnancy increases in size until it reaches its maximum in the third month of gestation and from this time on it is gradually absorbed. He calls attention to the fact that the vomiting of pregnancy disappears at about the time that the corpus luteum begins to decrease in size, and suggests that this is not a mere coincidence but that the corpus luteum plays an important part in relation to the vomiting. He has then developed a treatment for this disorder which consists of administering extract of corpus luteum. This treatment has been endorsed and recommended by many clinicians so that its use has become very widespread. On the other hand, many authorities will give this extract no credit at all, except in a suggestive way, for any beneficial results following its use.

The Carbohydrate Deficiency Theories

Hofbauer, in 1907, was the first to adduce evidence of a glycogen depletion of the liver which is "common" to pregnancy. Mottram shortly afterwards showed that a transitory fatty infiltration of the liver often occurred during pregnancy in nervous or ill-nourished animals and that such an increase of fat in the liver also occurred in some animals following a short period of hunger. Duncan and Harding believing a metabolic factor the cause of the vomiting of pregnancy and realizing that of the three protein, fat, and carbohydrate, the last was the most susceptible to disturbance were attracted by the work of Mottram while searching for evidence of such a disturbance. They came to the conclusion that a disturbance of carbohydrate metabolism existed because most patients suffering from this toxemia showed ketonuria and because they were able at the time to treat successfully over 70 patients by means of a diet rich in carbohydrate. They then in 1918 advanced the theory for the first time that a relative or absolute lack of glycogen in the maternal liver was the cause of the nausea and vomiting in pregnancy. In addition these workers advanced the opinion at this time that the periodicity so characteristic of Morning Sickness might be due to the same factor, viz., pregnancy and a short period of hunger which Mottram had shown led to a fatty infiltration of the liver.

This theory was more fully expounded by Harding in 1921. One of the functions of the placenta is to store glycogen for the foetus until the foetal liver is able to store its own reserve carbohydrate. During this period it is the glycogen of the maternal liver upon which it draws for its supply. At the end of the third month the foetal liver is fully formed and able to store its own glycogen. Then the drain on the maternal liver should cease.

According to Harding this drain on the glycogen content of the maternal liver occurs from the very onset of pregnancy and the early nausea and vomiting is an indication of the resulting deficiency in that organ. The continued and increased demand for glycogen on the part of the rapidly-growing foetus drains the glycogen content of the maternal liver. This deficiency causes nausea and vomiting and the vomiting results in inanation and

starvation with fatty infiltration and degeneration of the liver cells and ketonuria. The sudden cessation of vomiting in many cases at about the third month of gestation is claimed to be due to the fact that the foetal liver has reached full development and by storing its own glycogen relieves the maternal liver of the drain which is responsible for the vomiting.

A similar theory was advanced independently by Titus, Hoffman and Givens in 1920, but with a slightly different interpretation. They believe the deficiency of carbohydrate to be due to: (1) A relative deficiency brought about by unexpected demands on the part of the foetus and to a lesser degree by the hypertrophy of the uterus and (2) By an absolute lack of glycogen, augmented in the presence of nausea and vomiting, as the result of an improperly balanced diet.

The success of the theurapeutic measures founded on this carbohydrate deficiency theory have been convincing. Glucose therapy, particularly by the intravenous route as first exploited by Titus, led to a great improvement in the results obtained in the treatment of nausea and vomiting of pregnancy. That this starvation, with its dependent vomiting and ketonuria, was not the sole etiological factor soon became evident, however, as more cases were treated, particularly more severe cases. Other factor then came into prominence as a result of clinical and biochemical studies.

Chemical Findings.

The belief is very prevalent to day that the final solution of the etiology of the toxemias of pregnancy will result from metabolic studies and biochemical analysis. Most of the progress in the treatment of Nausea and Vomiting has come from such studies. It may then be advisable to review briefly the chief findings in the chemistry of the urine and blood in this toxemia and to consider the interpretations placed on any changes from the normal.

Before the advent of blood chemistry interest was largely centered on the urine of toxemic patients and various findings are on record. Stone in 1903 based his thory of "suboxidation" of protein on findings of a high residual urinary nitrogen. He claimed to have isolated from such urines crystals of leucine and tyrosine. Ewing and Ewing also found a high residual nitrogen but failed to co-operate Stone's crystals. It is now generally agreed that an analysis of the urine does not show any marked disturbance of the N partition except in severe cases, when an increase in the ammonia coefficient occurs. Williams was the first to observe this change and for a time regarded it as an index of the severity of the condition.

Ketonuria is common in pregnancy and it has been shown that the pregnant woman will develop ketonuria in a few hours on a carbohydrate-free diet. Harding believes that excretion of acetone parallels the clinical condition in vomiting of pregnancy. Harding and his co-workers also stress the importance of the specific gravity and the total daily amount of urine in patients suffering from this toxemia. This developed from their appreciation of the role of dehydration in vomiting. As severe cases were treated with glucose it was noticed that glucose alone might not bring about improvement, and that in these cases the total daily amount of urine was small while those which responded successfully showed coincident with the clinical improvement a greatly increased volume of urine with a lowered specific gravity. So much have Harding, Van Wyck and others been impressed with the value of this diuresis that they believe the successive treatment of Nausea and Vomiting depends primarily on the use of fluids and they relegate the use of glucose to secondary importance.

Urobilin or urobilinogen occurs in the urine of about 80 per cent. of cases

of nausea and vomiting. Berkeley, Dodds and Walker in 1924 brought forth evidence of the importance of these bodies as indications of hepatic damage during eclampsia, and claim the presence of these bodies in the urine is the earliest and surest guide we have of the presence of hepatic impairment. Harding was the first to recognize the value of urobilinuria in hyperemesis and has given to hepatic insufficiency a place in the etiology of Nausea and Vomiting. He has found that in cases improved by fluids that this urobilinuria disappears but that in those cases who still do badly despite diuresis that the urobilinuria persists. When there is no evidence of blood destruction then he believes the persistence of the urobilinuria means hepatic degeneration and, unless this is prevented by high calorific feeding to protect the liver, that the treatment is due to fail.

With the development of blood chemistry examination of its components has led to much specific information. Stander has found raised values for the nonprotein nitrogen and uric acid in severe cases. Harding and his co-workers found in addition an increase in urea and plasma proteins, with low values for sodium chloride. The blood sugar has received much attention and is apparently still unsettled. Dieckmann and Crossen reported the blood sugar to lie within normal limits and most workers have found this to be the case. Titus, on the other hand, insists that there is a hypoglycemia and assumes this is associated with the etiology of the disease. Dieckmann and Crossen found the hydrogen ion concentration and Harding and Stander the carbon dioxide combining power of the plasma to be essentially normal though existence of an acidosis has been postulated again and again and alkaline medication recommended.

It is now generally conceded that the raised values for the non-protein nitrogen, urea and uric acid are the result of dehydration. To this factor also Harding and Van Wyck attribute the low sodium chloride and deny the contention of Haden and Guffy that sodium chloride itself has any place in the treatment of hyperemesis. Finally increased values for the amino acids and for lactic acids have been reported. Arzt reports an achlorhydria of the fasting stomach contents in the majority of cases of Morning Sickness which he has studied.

Pathological Histology.

The pathological changes in the milder types of Nausea and Vomiting are quite unknown except as they may be interpreted from studies of the urine and blood.

Fifty years ago Mathews Duncan made a histological study of fatal cases and pointed out that pernicious vomiting is sometimes associated with definite liver lesions

Williams, Ewing and Stone, as a result of extensive autopsy studies, have directed attention to what they consider a characteristic type of liver lesion in severe cases of hyperemesis. This has since been described in text books as essentially a fatty degeneration or necrosis of the central portion of the liver lobule the periphery remaining intact. In more severe cases extensive areas of necrosis may occur closely resembling the lesion in acute yellow atrophy of liver.

These lesions are, however, probably not specific. Their close resemblance to those found in fatal cases of chloroform, arsenic and phosphorus poisoning has long been pointed out. More important now is the fact that starvation and dehydration alone produce typical liver lesions. The liver of fatal cases of hyperemesis as studied post mortem must then have the effects of those factors superimposed upon any lesions which may have been due to the toemia primarily. It is then very questionable if we are justified in speaking

of a typical liver lesion in Nausea and Vomiting.

The next most marked histological changes are to be found in the kidney. Here the pathological picture varies considerably. Most commonly found is a nephrosis evidenced by fatty degeneration of the epithedium of the secreting tubules, particularly of the convoluted variety. As a rule these renal changes occur only in the terminal stages of the disease.

As a result of these post-mortem findings the maternal liver has naturally held a prominent place in many theories regarding the etiology of this disease. The work of Opie, who pointed out that central and mid-zonal necroses of the liver are usually due to systemic poisoning lends considerable support to the toxemia basis of the Nausea and Vomiting of pregnancy.

Classification.

Williams originally classified the nausea and vomiting of pregnancy under three types — neurotic, reflex and toxic. In his latest text book he has dropped the reflex classification, and placed this as a subdivision of the neurotic type.

The reflex type, if it exists, must be relatively rare, as most obstetricians do not recignize reflex irritation as a cause of true Neusea and Vomiting. Most of those who do, consider it to include only the very mild cases, due to retroversion, long narrow cervix, a rigid os, constipation or adhesions. This type is frequently checked by simple suggestive measures. The success of such measures would seem to prove the condition is not essentially a pathological one.

The neurotic type is much more important. Kaltenback, in 1891, stated that vomiting of pregnancy is usually a manifestation of a neurosis, somewhat allied to hysteria and readily amenable to suggestion. Clinical observation has since afforded abundant evidence in support of such a view. Many workers will ascribe to neurosis as the sole etiological factor. The remarkable cures, even in women on the verge of death from starvation because of continuous vomiting, by the employment of the most varied and unscientific measures, or even the threat of an abortion, are well known.

The distinction between the neurotic and toxic types is hard to define and the two are interchangeable in many ways. The mere severity of the symptoms gives no clue as to whether a case is primarily neurotic or toxic. Williams believes every case rests on a toxemic basis and that variations in its course depend on the severity of the underlying toxemia, but that this factor merely acts as a predisposing cause in neurotic women, and becomes negligible after the neurotic element is controlled. Harding considers the toxic vomiting represents a certain stage in the course of the disorder and that its relation to the onset of the disorder is not a constant one, developing rapidly in some patients and slowly in others. It is safe to assume that a metabolic disturbance underlies all cases but to estimate the extent of the neurotic factor early. If the neurotic factor is not appreciated early and treatment instituted for it the continued vomiting will result in starvation and dehydration so that one is now dealing with a true toxic case whatever may have been most important in initiating the condition.

Clinical Course.

It is convenient to divide cases of Nausea and Vomiting into mild and severe, whatever their type—neurotic or toxemic. A mild case is the well-known Morning Sickness, in which the patient suffers from nausea, with or without vomiting, usually in the early morning before arising. Later in the forenoon the nausea passes off for the rest of the day to return at the same time next morning. In other cases the nausea does not appear in the morn-

ing, but occurs later in the day, and tends to be repeated at this time each day. In such mild cases there are no injurious effects on the patient's health and she may recover at any time.

Mild cases may, however, pass insensibly into the severe or pernicious type. Now the patient loses her appetite and the stomach becomes more and more intolerant to food, so that even a mouthful of solid food or water may not be retained. Actual loathing of food may occur, so that the sight or mention of it may be sufficient to give rise to violent retching. Emaciation and dehydration are inevitable. Dehydration may be evident only by slight dryness of the skin and thirst. This stage may last several weeks or only a few days. In either event a critical point has been reached. Thalhimer, Polak and others believe that once dehydration is established a vicious circle is set up—starvation and dehydration leading to acidosis, acidosis to increased intolerance of the stomach and more nausea and vomiting. Titus, Harding and others do not subscribe to this view of an acidosis but believe the importance of this stage of acute dehydration lies in the fact that at this stage administration of fluids alone will replace the loss of water, but will not once chronic dehydration is established with its resultant destruction of the formed and colloidal elements of the blood.

Whatever the more important mechanism, if the dehydration is allowed to persist chronic dehydration is inevitable with its classical signs of a weak thready pulse, pale mucus membranes, and low blood pressure. A low value for the serum proteins will now be found and prognosis is very grave. The patient is now in an extremely pitiable state. She is vomiting consistently, there are sordes on the teeth, the lips are cracked, the tongue dry and red, and the vomitus may be flecked with blood. Finally the serious symptoms of liver degeneration appear. Jaundice, rising pulse, and low fever are followed by a terminal stage lasting only a few days or hours. The vomiting ceases, the pulse is rising, the temperature rises, liver tenderness and deep jaundice appear, then delirium, coma and death.

Diagnosis.

When confronted with the symptoms of nausea and vomiting, associated with amennorrhea, it is of course necessary to determine whether there is any other cause for these manifestations. At least the more common causes of pathological vomiting, such as gastric ulcer, acute intestinal obstruction or the onset of an acute infection, should be remembered. A careful history and physical examination are then essential. Having satisfied oneself that the case is one of true Nausea and Vomiting of pregnancy an attempt should be made to estimate how great is the factor of neurosis and to what extent the various sequelae of vomiting have progressed. A 24-hour specimen of urine will reveal the presence or absence of dehydration, its presence being indicated by oliguria and high specific gravity. One specimen may reveal the high specific gravity — 1030 or so—but this is never reliable, as the specific gravity depends on whether the process of dehydration has been acute or chronic. A dehydration produced slowly will give only a moderate rise.

The presence or absence of starvation can be determined by testing the urine for acetone bodies, and this should always be done. If the ordinary tests are negative for this substance there must necessarily be only a slight degree of vomiting. In this case if severe symptoms are complained of the case must necessarily be classed as neurotic.

Treatment.

With the numerous theories of etiology proposed for this disease it is natural that there should be no unanim-

ity of opinion regarding its treatment. The theory of Hirst has led to extensive use of extract of corpus luteum. Carey has employed dessicated placenta. Garnet recommends transfusion from post partum patients. Luikhardt proposes luminol for its effect in allaying vomiting. Many others believing principally in the neurotic element treat their patients largely by suggestion and the use of sedatives. The theory of glycogen depletion has led to widespread use of carbohydrate, with and without insulin.

Obviously, all these measures cannot be utilized in any one theurapeutic plan. With realization of the abundance of controversy on the subject one must try and pick his way in places of fairly well recognized security. For this reason the outline given below is based on that originally expounded by Harding and Watson and is in its essentials that in use at Toronto and in the clinics of Williams, Titus, Spiedal and many others. Its main difference from those of other prominent methods of treatment will bediscussed later.

(a) Treatment of Mild Cases.

The treatment of a mild case of Nausea and Vomiting — one still ambulant and not showing any injurious effects, —is relatively simple. In many cases the first thing tried will be successful. More often success will be found to depend upon various factors, none specific, and all apparently minor ones, but which when happily combined lead to a rapid cure.

The first essential appears to be marital abstinence, and a separate room for the patient should improve matters considerably at once. Rest, with relief from the preparing of meals should be carried out as far as possible. Full meals are better replaced by 6-7 small meals a day with decreased fatty food and increased carbohydrate in any form. Fluids must be urged up to several quarts a day. Regulation of the bowels is important as constipation alone may nullify the good results of all the rest of the treatment. Here one may have to rely on enemata or pills as anything else may cause nausea. The only other drugs required are small doses of bromides several times a day. The treatment of mild cases of Nausea and Vomiting is largely an individual matter in each case, so that apart from a few such hygienic and dietetic rules the individual adaptments which the physician is able to make for each patient are probably the most important factors in achieving a cure.

(b) Treatment of Severe Cases.

If the Nausea and Vomiting fail to yield to such simple measures the condition takes on the aspect of hyperemesis and extreme and vigorous theurapeutic measures should be delayed no longer. There are certain well defined and tried procedures in the treatment of this distressing condition which can be safely carried out even in the home, and these should be instituted without delay. Isolation in a hospital, with private room and private nurse is ideal, but if this is not possible much can be done in this very important detail at home, by the choice of the brightest room far from the kitchen and the exclusion of all visitors, including the husband. After preliminary morphia to ensure rest the starvation and dehydration must be combatted. This is best done by the administration of 5 per cent. or 10 per cent. glucose in saline by the intravenous route. No food is given by mouth for at least 24 hours, then fluids are urged. The intravenous therapy is repeated daily until the acetonuria disappears and there is over a litre of urine daily with a specific gravity of 1010 or less. Titus uses more concentrated glucose than most of the other men, giving 50-75 grams of glucose as a 25 per cent. solution 1-3 times a day. Regulation of the bowels as in mild cases and sedatives are essential. The latter may well be given rectally. By the third day small, well prepared,

carbohydrate meals should be retained. Oral administration of fluids must not, however, be discontinued under any condition. If urobilin persists in the urine after a few days of such treatment liver degeneration is occurring. The duodenal tube, kept in place by the nasal route, with high calorific feedings every two hours will usually protect the liver and cause disappearance of the urobilin.

If after a reasonable period of such treatment, usually a week, acetonuria, oliguria, or signs of liver degeneration such as urobilinuria or jaundice are present theurapeutic abortion is usually done. This is very rarely necessary, but if it is refused for religious reasons repeated blood transfusions, with persistence of the duodenal and intravenous therapy may still turn the tide.

This plan of treatment makes no mention of two things in particular over which there is considerable controversy in the literature, namely, the use of alkalies and the use of insulin.

Wilson advocates sodium bicarbonate with the intravenous glucose on the grounds that the carbon dioxide cambining power of the plasma is generally low in hyperemesis, and that though glucose will raise the alkali reserve it can be raised more quickly if carbonate is added. Most workers, however, believe that the carbon dioxide combining power is rarely significantly low and that alkali administration then carries an element of danger with it.

Thalhimer advocates the use of one unit of insulin for every three grams of glucose given. He believes that true acidosis exists in hyperemesis, based on the finding of a much lowered plasma bicarbonate in his laboratory. He believes that the acidosis causes vomiting and that insulin by enabling the body to oxidize glucose causes complete metabolism of the acetone bodies. He has found many supporters for this view and insulin is quite extensively used in hyperemesis. The rationale of this therapy is vigorously opposed by Titus, Harding, MacLeod and Campbell and others, on the ground that a true acidosis does not exist and that the presence of acetone bodies is the result of lack of glucose and not the failure to oxidize it. Titus, with his findings of hypoglycemia in pernicious vomiting, believes the use of insulin to be dangerous as the desideratum is storage of glucose in the liver cells and not its combustion.

Summary.

1. Nausea and Vomiting of Pregnancy is never physiological.

2. Mild cases should be treated with energy because:

(a) The treatment is purely medical and the measures simple.

(b) This is the only method we have of preventing the serious condition of hyperemesis.

3. A metabolic disturbance, the exact starting point of which is unknown is the most plausible theory of its etiology.

4. Great improvement has resulted in the treatment of mild and severe cases from recognition of the four factors so admirably emphasized by Harding, namely, starvation, dehydration, liver degeneration and neurosis.

5. Insulin and alkalies are unnecessary.

Recent Advances in the Treatment of Pulmonary Tuberculosis.

By W. S. STANBURY, B.A., M.D.

While Trudeau's advocacy of sanitorium rest still remains the chief contribution of modern medicine to the treatment of phthisis, recent years have brought forward a considerable measures promising to further delimit the inroads of disease. Chief among these has been the introduction of collapse therapy by means of the artificial pneumothorax. Although the method was suggested as early as 1822 by Carson of Liverpool, it is only within the past few years that this form of therapy has received universal approval. Space will permit but the barest outline of the present problem. Recognizing the pleomorphic nature of pulmonary tuberculosis, with its impalpable factors of activity and host resistance, it will at once be evident that each patient will present an individual problem in therapy. This fact cannot be too strongly emphasized in the consideration of the general schema herewith presented.

Artificial Pneumothorax.

Statistical treatment alone gives but a meagre conception of the benefit resulting from this single form of therapy. It is therefore of utmost importance that everything should be done to abolish the timidity in the public mind, and even yet in the minds of a few of the profession, towards artificial pneumothorax as a safe and efficient form of treatment for pulmonary tuberculosis. True, it should be avoided where possible, but certainly not in suitable cases where there is a reasonable doubt as to how efficiently the patient will react to ordinary rest treatment. The general indications for collapse therapy might be summarized briefly as follows:

A. Unilateral Tuberculous Lesions, — where

1. Progressive unilateral disease not responding to ordinary sanatorium bed rest. Temperature, pulse and body weight in patients so benefitted should show a tendency to return to normal within eight to ten weeks after admission. Evidence of recent extension, either radiographic or by physical signs after this period, even where toxemia is abating, demands that collapse therapy be considered. (Wingfield.)

2. Acute pneumonic disease definitely confined to one lung. It is probably wise to always attempt artificial pneumothorax in these cases, with the hope of limiting spread.

3. Uncontrollable Hemoptysis: Provided the source of bleeding can be definitely shown to be in one lung, both from the sensations of the patient and the presence of bubbling rales, a penumothorax offers the best hope of prompt control. Induction of a "continuous pneumothorax" on two patients at Calydor Sanatorium was probably directly responsible for a favourable outcome. This method, designed by Dr. C. D. Parfitt, is effectual in the continuous application of sufficient positive pressure over the bleeding lung. In one of the above cases this was maintained for a period of ten days, reaching a maximum pressure of 70 cm. of water. Those patients with relatively fixed mediastinums tolerate this form of treatment with less cardio-respiratory distress than others.

4. Quiescent unilateral disease with incomplete response to routine sanatorium treatment. This group will include those who have not quite regained their normal health, or who on account of cavities, still expectorate large quantities of sputum. This latter situation is worthy of serious consideration, for as Wingfield has clearly shown persistence of positive sputum militates against the patient's further improvement. There is also a considerable group on whom economic conditions enforce the shortest periods of

sanatorium treatment practicable and for these individuals artificial pneumothorax offers a greater margin of safety.

5. Complications such as tuberculous larnygitis and gastrointestinal symptoms due to tuberculous toxemia are frequently relieved by the induction of artificial pneumothorax.

6. There still remains for consideration that group of lesions, other than the pneumonic types, which might with good reason be treated immediately by pneumothorax without preliminary sanatorium rest. On this question widely divergent views are expressed. Burrell states dogmatically that with few exceptions unilateral lesions of an area corresponding to two ribs and interspaces showing bacilli in the sputum, should be treated with pneumothorax immediately. Generally speaking collapse therapy is practised more conservatively here than in Europe. In doubtful cases, however, it is wise to err on the safe side and induce pneumothorax.

B. Bilateral Tuberculous Lesions.

Where one lung is much worse than the other collapse frequently not only removes evidence of toxemia, but is followed by much improvement of the lesion of the opposite side. This group of cases requires much more careful selection than the above. The degree of activity present in the other lung, rather than the actual amount of disease is the first consideration. Generally speaking extensive involvement of the opposite lung, other than at the apex is a contraindication for pneumothorax.

Simultaneous bilateral pneumothorax has at the present time many advocates. It has probably a very limited application, and in the vast majority of suitable cases greater benefit would ensue from collapsing one and at a later date the other lung.

C. Replacement of Pleural Effusions.

As to the advisability of aspiration with replacement by air in cases of idiopathic pleurisy with effusion there is a wide divergence of opinion. It is the practice at Calydor Sanatorium, and has, it is felt, many distinct advantages. In the first place, accepting the dictum of tuberculous etiology in these cases, it is wisdom to preserve the pleural cavity for therapeutic pneumothorax if deemed necessary. Secondly, the introduction of even a small amount of air allows the fluid level to be watched with accuracy. It is impossible in every case even for those greatly experienced in the use of the fluoroscopic screen, to differentiate fluid from thickened fibrinous pleura without the presence of an air bubble as guide. Thirdly, the introduction of air seems in many cases to arrest further exudation.

The aspiration of effusions complicating artificial pnenmothorax is another vexed point. If allowed to persist they must be carefully watched, for there is a definite tendency for adhesions to form at the base, and for the process to progress upwards to the obliteration of the whole pleural space.

The chief consideration in the contemplation of pneumothorax therapy is the condition of the other lung. Active bilateral disease need only be taken as a contraindication if collapse aggravates the disease in the opposite lung, or if the lesions are so extensive that simultaneous or alternate collapse of both lungs is not feasible. The presence of intercurrent disease such as asthma, emphysema, and uncompensated heart lesions will usually eliminate consideration of this form of therapy on account of attendant dyspnoea, papitation and cyanosis. Contrary to the opinion of Lawrason Brown, we have observed diabetics benefit greatly by collapse therapy, combined with dietetic control and the use of insulin.

The mishaps attendant on operation are so very rarely of serious moment, or so insignificant in nature that they can hardly be considered contraindications to a form of treatment offering such dramatic benefit. The most serious of these is the so-called pleural shock, manifested by slight faintness in mild cases and more rarely by actual sudden death. Stivelman could find only one fatal case reported in a series of 10,141 pleural punctures by American physicians. Extreme mental agitation amounting almost to terror was in all probability a factor in the only fatal case of the Calydor series. The patient, a highly excitable French-Canadian, expired with dramatic suddenness as the anaesthetic needle was felt to reach the parietal pleura. Wingfield was unable to find in the literature any irrefutable evidence for the occurrence of gas embolism as a complication of artificial pneumothorax, and certainly if it does occur it rightly belongs to the historic period of collapse therapy, before the manometer became indispensable to the proper management of the patient.

The actual technique of collapse therapy cannot here be dealt with in detail. The Saugman type of pneumothrax apparatus will be found quite satisfactory and very simple to manipulate. Further it may readily be improvised in an emergency. A gradual induction without any marked temperature reaction is of great importance. After thorough anesthetization of chest wall and parietal pleura with novacaine, a blunt needle of the Riviere type or that of Kuss is introduced into the pleural space. When the manometer indicates by its free movement with inspiration and expiration, that the needle point lies within the pleural cavity, the patient is allowed to aspirate as much air as possible before any positive pressure is exerted on the pneumothorax apparatus. Only a small amount of air, about 300 c.c., is introduced on the first occasion, the operation being repeated in 24 hours and again in 72 hours. The interval is gradually lengthened as the desired degree of collapse is obtained, so that refills will only be necessary at intervals of a fortnight or more in order that the intrapleural pressure may be kept reasonably constant. Bed rest after the early refills is essential. In pneumothorax therapy the maintenance of an optimum pressure for the individual is the crux of successful treatment. This will be found to vary considerably, many patients doing best on partial collapse. The English clinicians lay great stress on loss of body weight, increase of pulse rate and the development of an irregular or periodic type of temperature curve as indications for the necessity of readjustment of intrapleural pressure.

It is very difficult to state how long one should persevere with artificial pneumothorax treatment in the favorable case. Saugman believes 5 years a minimum. Generally speaking the process of natural obliteration should be well in hand,—thickened pleura, sinking chest wall, displacement of the mediastinum, and gross pulmonary fibrosis with shrinkage. In Wingfield's large series, duration of treatment averaged 3-5 years. In patients not responding so favourably to treatment, one is justified in maintaining even a very partial collapse if by so doing the case is benefitting symptomatically.

Although as has already been stated statistical enumeration is hardly a fair representation of the great therapeutic value of artificial pneumothorax in pulmonary tuberculosis, in that it is so frequently employed as a palliative measure in far advanced disease. the results of Matson and Bisaillon on 492 cases of all types may be of interest. No cases then under treatment, or receiving refills within a two-year period were included. Of all cases obtaining a satisfactory collapse 44.8 per cent. were clinically well, 15.6 per cent. arrested, and 28.8 per cent. died, while in the control group represent-

ing those in whom the induction could not be accomplished, 4 per cent. were clinically well, 12 per cent. arrested and 63.8 per cent. dead. The most striking results are obtained in the unilateral fibro-caseous disease with little or no cavitation.

The most frequent complication arising during pneumothorax treatment is the development of a pleurisy with effusion. Some effusion probably takes place in all cases, but in from 40 to 50 per cent. of pneumothorax patients an effusion is clinically apparent. The onset may be alarming, in that the symptomatology frequently suggests the acute exacerbation of disease thought to be in the process of arrest. Other than the ever present danger of obliteration of the pleural cavity by adhesions, this complication cannot be regarded as serious. In fact pleurisy with effusion may be followed by rapid clinical improvement. It is the usual result, following effusion to find a partially expanded lung more completely collapsed, and a flexible mediastinum with greater fixity of position. Should the effusion become purulent, however, it is very much more serious. With a lung showing no sign of re-expansion, provided of course the condition of the other lung and the patient's general health warrants such a measure, thoracoplasty with or without phrenic evulsion should be done as soon as possible. In those cases where an obliterative process is proceeding inexorably, the induction of oleothorax has been suggested as a means of preserving the pleural space. This procedure consisting of the introduction of 5 per cent. gomenol in olive oil is, however, not usually a success for depression of the diaphragm by its weight and bulging of the mediastinum too often prevents the filling of the cavity. There is rarely any advantage in maintaining a small pneumothorax cavity, and where collapse is still considered desirable thoracoplasty must be considered. Gomenol moreover is badly tolerated by some individual, causing severe reactions.

Adherent pleura and bands of fibrous tissue are by far the most frequent causes of failure in pneumothorax therapy. Where bands of adhesions are preventing satisfactory collapse, one should endeavour to stretch these gently by small and frequent refills. High positive pressures are ineffectual and dangerous. The open operation of thoracotomy for section of these adhesions has been suggested but cannot be considered a safe and effective form of treatment. In all five Calydor patients undergoing this operation a pleural effusion developed, two of them becoming tuberculous empyemata. Nor can the division by cautery under the direct vision of a thorascope, advocated by Jacobaeus, be pronounced free from danger. Section of an adhesion with a core of lung tissue is frequently followed by severe hemorrhage or spontaneous pneumothorax with empyema. For these cases thoracoplasty is by far the safest operation.

Thoracoplasty.

The thoracoplasty or extrapleural paravertebral rib resection of Sauerbruch is an operation designed to produce permanent compression of the underlying lung. The very nature of the operation demands the most careful study of the individual patient before it is undertaken. The chief indications for this more radical form of treatment might be summarized briefly as follows:

1. In tuberculous empyema, especially in those cases associated with spontaneous pneumothorax, a thoracoplasty should be performed as soon as it is clear that the lung cannot re-expand, and while the general health of the patient is still unaffected.

2. Where artificial pneumothorax would ordinarily be indicated but cannot be effected on account of pleural adhesions, or where it has not been possible to maintain a satisfactory col-

lapse for various reasons already suggested. One should never conclude from the radiological picture or from a history of pleurisy that the induction of pneumothroax is impossible. It should be attempted in all suitable cases. Although in the Calydor series there are about 45 per cent. failures in the cases attempted even these are of distinct advantage to the surgeon in warning him of the condition of the pleura. A preliminary even partial pneumothorax will on the other hand tend to further fibrotic changes, render the mediastinum less flexible and extend to the opposite lung a period of probation. It has been noted in the Calydor series that where a pneumothorax existed for some time previous to the operation a better collapse was more readily obtained and that the postoperative symptoms were usually less marked.

The necessity for careful selection has already been emphasized. Evidence of resistance as judged by the changes in the bad lung, the condition of the opposite organ and to a lesser extent the age of the patient is of extreme importance. Fibrotic changes and contraction with definite displacement of the mediastinum will indicate a relatively high degree of resistance even in those cases with some recent extension of disease. Those lesions with little evidence of fibrotic change must be considered very doubtful risks often however benefitted and rendered suitable for the more radical operation by even partial pneumothorax over a prolonged period or occasionally by phrenicotomy. Healed processes in the opposite lung generally indicate high local resistance. Generally speaking lesions when present in the better lung should be radiologically minimal in extent, and physical signs should be very slight or absent. While the patient's age is no absolute contraindication to operation it has been found in the Calydor series that results improved proportionately in each age group up to twenty years from the onset of disease.

Severe kidney disease or uncompensated heart lesions must be considered contraindications to operation. The operation must not be done as a last resort, but only when the patient's general health and vitality are at their best. Archibald has pointed out that one can hope for only partial or temporary improvement where there is considerable cavitation in both lobes.

The operation is yet too recent a development to give a just picture of its acknowledged benefits. In the Calydor series of 25 patients extending over a period of 12 years, 72 per cent. obtained good results following operation, 44 per cent. of these becoming arrested, and to the present 56 per cent. have maintained their position. Only one patient has died as a result of the operation, and one made worse by the development of a streptococcal emypema.

Phrenicotomy.

Although phrenicotomy has been considered a therapeutic measure of minor importance by many clinicians, the series of 49 operations at Calydor Sanatorium would seem to show distinct benefit not only in those rarer basal lesions, but in a certain number with apical distribution. In all but eight cases the phrenic evulsion of Felix was the operation of choice. Experience has taught that this is the only certain method of producing diaphragmatic paralysis for in about 25 per cent. of cases the existence of an accessory phrenic nerve has been noted. The operation may be done under local anethesia but considerable pain on the withdrawal of the nerve frequently makes gas or oxygen or sodium amytal desirable. Incidentally this latter introduction into anesthetic methods has proved a great boom to those operating on the pulmonary case.

Many of the indications for phrenicotomy have been noted during the early part of this paper. Although as a

means of controlling or arresting disease this form of therapy cannot be considered in the same class as pneumothorax or thoracoplasty, yet it has proved of benefit in a considerable number of cases in whom more drastic interference is either inadvisable or impossible. In a group of 21 patients undertaken for this reason, marked success was achieved in 10, partial success in 5. and in only 6 was the operation considered a failure. Twelve apical lesions were distinctly contracted, two of these showing almost complete obliteration of large cavities.

Frequently the operation is of value in the removal of troublesome symptoms such as cough, tachycardia and dyspepsia, and occasionally is successful in controllng recurrent hemoptysis. In 5 out of 8 cases in this group, the objective was attained, although it failed to prevent the subsequent return of hemoptysis in one case.

The operation has already been mentioned as an accessory to artificial pneumothorax in lessening the frequency of refills, in controlling effusions and in giving greater stability to the mediastinum. In three out of the eight cases attempted the operation could not be said to be of any value, but marked success was achieved in two instances.

Occasionally phrenicotomy may be successful in the control of tuberculous empyemata or persisting pleural effusions. Success was attained in two of the three cases undertaken for this reason.

Phrenic evulsion is now employed almost universally as a supplementary operation to thoracoplasty. Dr. N. S. Shenstone believes that the best results are obtained by performing evulsion several months before or at an equal interval after the major operation.

Finally, the operation may be of value as a precautionary measure in the prevention of relapse after a patient has left sanatorium.

Summary.

In this paper I have attempted to outline those measures, artificial pneumothorax, thoracoplasty and phrenicotomy, which in recent times have proved of greatest benefit in supplementing the routine sanatorium treatment of pulmonary tuberculosis.

At the Calydor Sanatorium, during the fourteen years since 1916. compression of the lung by artificial pneumothorax has been attempted in 177 patients, that is in 21 per cent. of all tuberculous patients under treatment, thoracoplasty in 25 cases or 3 per cent. and phrenicotomy in 49 or 6 per cent. making a total of 28 per cent. of all tuberculous individuals under treatment in this sanatorium for whom these supplementary surgical measures were deemed advisable. Space will not permit a review of the chemotherapeutic and dietary measures recently suggested in the literature. Sufficient be it to say that of the former we have found Moellgaard's sanocrysin (gold-sodium-thiosulphate) of definite value in certain selected cases. These two fields of therapeutics may prove of great importance in the near future, for with the interesting work of McConkey and Smith on the value of vitamines A and C in resistance to tuberculous infection and spread, and the encouraging reports of the Sauerbruch clinic on the use of highly spcialized diets in surgical tuberculosis, a new era in phthisical therapy may well be at our door.

I take this opportunity of thanking Dr. Parfitt for his kindly criticism in the preparation of this communication, and for the free access to the clinical records of Calydor Sanatorium.

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Bacterial Endocarditis (Continued)

By J. A. DAUPHINEE, M.D.

Cerebral Lesions.—The most serious embolic lesion that may occur is the plugging of a cerebral vessel. The most common clinical result of cerebral embolism is hemiplegia with aphasia if the hemiplegia be right sided. Monoplegias are much less common. The resulting cerebral shock is usually considerable. Sudden blindness may occur from the plugging of the central artery of the retina. Retinal haemorrhages may be present and indicate smaller emboli.

Other Vascular Lesions.—The occurrence of embolism in large peripheral vessels is not a very uncommon event in the course of subacute bacterial endocarditis. Blumer (1923) for a series of 300 cases noted the following frequency and situation of such a lesion:

(1) Arteries of the upper limb were embolic in 13 cases.

(2) Arteries of the lower limb were embolic in 10 cases.

(3) The radial, foot, and brachial arteries were by far the most frequently attacked.

(4) Other situations for emboli attacked rarely were the popliteal, leg, nasal, internal carotid, aorta, renal, axillary, and mesenteric arteries.

An occasional sequel to such an embolism is the formation of a mycotic aneurism. Horder (1926) states that quently in the left hypochondrium, he has twice seen embolism of a mesenteric artery—as shown during life by a sudden attack of severe abdominal pain. The coronary arteries are rarely involved.

SYMPTOMS AND DIAGNOSIS.

These will not be discussed in any detail. Most of the important symptoms and signs have already been referred to. Bearing these in mind, there should be little difficulty in making a diagnosis. The signs of an endocarditis, clubbed fingers, multiple embolism and an otherwise unexplainable anaemia and cachexia constitute a syndrome which scarcely admits of any other conclusion.

The only manifestations of a subacute bacterial endocarditis may be those of a low grade toxaemia, the patient complaining of lassitude, anorexia, pains in the extremities, feverishness, headache and perhaps occasional cardiac discomfort. The onset may be more abrupt and acute with high fever, chills and sweats. Later, pallor, pigmentation of the skin and emaciation are present. There may be tenderness of the lower end of the sternum and clubbing of the fingers. As the disease progresses embolic phenomena appear such as petechiae on the conjunctiva, face or upper portion of the chest. Abdominal pain, which occurs most fre- splenic tenderness, and enlargement of

spleen and liver are frequently present. Tender nodules about the pads of the fingers and toes are almost pathognomonic.

Cerebral lesions evidenced by sudden loss of consciousness hemiplegias, muscular twitchings, facial and ocular palsies and sudden blindness due to embolism of central artery of the retina may occur. There may be praecordial discomfort due to cardiac involvement. Melena occurs in certain cases. Gangrene of an extremity due to embolic obliteration of an artery has also been described.

PROGNOSIS.

The duration of the disease has already been discussed with the bacteriology. The outcome is practically always death. The duration will be long or short, depending upon the organism, the general resistance of the patient and the occurrence of cerebral accidents. Libman, however, has called attention to the fact that accasionally patients with undoubted subacute bacterial endocarditis get well and have a very good expectancy of life. Four of his first 150 cases recovered (1925-26). Altogether he reports that he has records of at least 10 complete recoveries. Other isolated instances of recoveries have been reported, but such are extremely rare and a diagnosis of a bacterial endocarditis carries with it a very grave prognosis.

CAUSE OF DEATH.

In the subacute type, Clawson (1924) found various causes of death, including cardiac failure, sepsis, cerebral embolism and pneumonia, but by far the most common cause was cardiac failure. In the acute class, secondary to some obvious acute focus, the causes were more varied, including cardiac phthisis, peritonitis, diabetes, myeloid failure, sepsis, accident, military tuberculosis, carcinoma, pneumonia, chronic leukemia and Addison's disease. The chief of these was sepsis. In the primary acute class cardiac failure again predominated.

Horder (1920) in discussing subacute bacterial endocarditis states that death may occur from toxaemia, heart failure, uremia, or cerebral or coronary emboli. Cotton (1920) reports 26 deaths from gradual heart failure, 5 from acute heart failure 3 from hemiplegia, 1 from pulmonary embolism, and one from a streptococcal pneumonia. Starling's series (1922-23) show that 13 died of heart failure, 5 of renal insufficiency, 3 of arterial embolism and 1 after operation for intestinal obstruction. In Rost and Fischer's (1928) series of children the cause of death was most frequently cerebral embolism. Some died from cardiac and renal insufficiency and some from intercurrent infection.

From Blumer's analysis of 193 cases the main probable causes of death were:

(1) Cachexia or exhaustion (toxaemia), 30%.

(2) Chronic cardiac insufficiency, 24%.

(3) Cerebral embolism, 21%.

These three conditions represent 75% of the probable causes of death in subacute bacterial endocarditis.

TREATMENT.

Just a brief word will be said about the treatment of bacterial endocarditis. No form of therapy so far has shown any evidence of influencing the course or duration of the disease. Autogenous vaccines, arsenicals, serums, blood transfusions have been without permanent benefit. Horder (1926) has tried arseno-benzol and sodium cacodylate with little discernible effect and has had just as little success with immuno-therapy.

Our main hope lies in prophylaxis. Prevent Rheumatic Fever. In those that have damaged valves care should be taken to prevent the occurrence of foci of infection, and any such should be eradicated. The general health and

resistance should be built up by proper diet and hygiene. Care should be taken to prevent respiratory tract infections and other such which may lower the general resistance and serve as a starting point for a bacterial endocarditis.

COMMENT.

The following case will be seen to present most of the features of the condition known as subacute bacterial endocarditis as defined by Libman (1912). We find that the patient was admitted in June, 1921, for the first time, with malaise and headache and no previous history of rheumatic fever. His heart showed some enlargement to percussion and he was found to have an aortic regurgitation. He showed no evidence of cardiac failure, but did show shortness of breath on exertion. He was discharged in good health with a diagnosis of erythema multiformes, aortic regurgitation, and chronic tonsillitis. All of which were probably evidences of rheumatic fever.

He then carried on with light work for seven years, when he had an attack of what was obviously rheumatic fever. Five months after this he was suddenly stricken unconscious, and when he regained his senses two hours later he was unable to talk.

Examination on admission to hospital at this time showed marked enlargement of the heart with diastolic murmur to left of the sternum and at the apex. There were other marked signs of aortic regurgitation. There was no clubbing of the fingers, but the nails seemed somewhat cyanosed. The patient was conscious, but could not speak. There was definite weakness of the lower facial muscles on the right side. The tendon reflexes were normal. The clinical diagnosis was Aphasia due to embolism, chronic myocarditis — rheumatic, chronic endocarditis, and aortic and mitral insufficiency. The laboratory findings showed nothing abnormal at first, but a slight anaemia. The orthodiagram showed some enlargement of the heart.

He gradually improved until the end of June, when one month after his admission, with signs of cerebral embolism, he developed a small purplish area in the tip of the right index finger which was tender. A week later the spleen was enlarged and palpable and red blood cells were found in the urine. At this point an additional diagnosis of subacute bacterial endocarditis was made.

The diagnosis would certainly seem at this point to be amply justified even in the absence of a positive blood culture at that time. Here is a man who has had rheumatic fever who suddenly develops signs of cerebral embolism. Such rarely occurs in rheumatic fever except in a case where the heart beat changes from aricular fibrillation to a normal rhythm. This man's heart was quite regular at all times. Then he develops a tender palpable purplish area in the end of a finger (Osler node) and at the same time his spleen becomes palpable and red cells are present in his urine—evidence of the focal nephritis or renal infarct described before.

The progress from that time on was progressively downward. A positive blood culture of anhaemolytic streptococci was obtained about one month after the development of the first Osler node. Two more Osler nodes developed. Blood was found more or less constantly in the urine and his fundus showed evidence of retinal haemorrhage.

Four months after the first cerebral embolus the patient developed signs of a second such lesion, showing great difficulty in speech and some mental confusion. The heart was enlarged. The liver was enlarged and there were rales in the lung bases. The spleen was easily palpable and tender. Petechial haemorrhages were present in the right palm and there was slight evidence of clubbing of the fingers. The anaemia was more marked, but the white count remained normal. A few days later the

petechiae were more numerous, signs of heart failure more prominent—with fluid and shifting dullness in the abdomen. His condition quickly became worse and he died.

The clinical picture, then, was that of a man with previous rheumatic heart disease and aortic insufficiency, who developed a cerebral embolus, followed by Osler's nodes, palpable tender spleen, evidences of nephritis, retinal haemorrhages, positive blood culture, petechial haemorrhages, and died from the effects of a second cerebral embolus and heart failure. The final clinical diagnosis was subacute bacterial endocarditis; chronic myocarditis, rheumatic; chronic endocarditis, rheumatic, with mitral and aortic insufficiency; cardiac hypertrophy; cerebral embolism with right hemiplegia; and nonthrombopenic purpura, symptomatic.

On autopsy the clinical diagnosis were justified. The skin showed evidences of petechial haemorrhages. There was a massive area of haemorrhage on the anterior pole of the temporal lobe about the Sylvian fissure, although no emboli were found in the main vessels of this area. Serial section of the left cerebral hemisphere revealed one area of haemorrhage extending for about 2 cms. into the Sylvian fissure. The brain substance below this area was extremely mushy and soft in consistency. This was the lesion that probably accounted for his aphasia —involving Broca's area.

The lungs showed marked congestion. the pleural, pericardial and abdominal cavities showed marked effusions —evidences of myocardial insufficiency. The heart itself showed marked enlargement of the left ventricle. The aortic valves were encrusted with massive vegetations which were greenish grey in color. The valve cusps were diffusely thickened throughout and one showed a fenestration probably due to ulceration. The mitral valve as well showed massive vegetations on thickened cuspc. The heart muscle showed evidence of recent and old inflammatory processes. There was marked increase in the interstitial and perivascular fibrous tissue. There was a slight perivascular infiltration of lymphocytes with a few scattered endothelial cells in some areas. No Aschoff bodies were found. There were no mural vegetations, but the endocardium of the left auricle showed, however, a finely wrinkled appearance in some areas and appeared somewhat thickened.

The liver and spleen were moderately enlarged. The spleen showed pyramidal areas, with the base at the periphery, of old and recent infarction.

The kidneys showed evidences of petechial haemorrhages beneath the capsule and in the cortical zone as well as triangular areas of old infarctions. In addition to a chronic lymphocytic infiltration of the interstitial substances, many of the glomeruli showed evidence of complete or partial fibrosis similar to that described by Baehr (1912).

From this brief resumé of the clinical history and autopsy findings it is seen that the case presented most of the features of what has been termed subacute bacterial endocarditis. True, the autopsy diagnosis calls the vegetative lesions "acute," but according to Clawson (1924) the vegetative lesions of the 'subacute acute" form cannot be distinguished in the gross from the "acute" forms. The fact that the lesion is "ulcerative," too, does not rule out a subacute or chronic lesion. Certainly from the history of the case which dates positively to four months before death, the disease could hardly be classed as acute. The evidence of scarred infarcts also points to a fairly long standing process. The classification depends upon a clinical or pathological definition of the word acute.

The pathological report also gives a diagnosis of "healed ulcerative endocarditis," but just why this diagnosis was made rather than a "chronic rheumatic endocarditis," is not clear from the description in which the valves are described as being "diffusely thickened throughout." There is further evidence

of previous rheumatic endocarditis in the thickening and wrinkling of the mural endocardium of the left auricle (Clawson and Bell, 1926).

The demonstration of the results of emboli in brain, kidney, spleen, skin and gastric mucosa all agree with the clinical picture. The presence of the embolic type of nephritis is also characteristic of subacute type of bacterial endocarditis.

CONCLUSION.

A brief description of the bacteriology, aetiology, and pathology, of bacterial endocarditis has been given. The most frequent form of the disease is the subacute or chronic type which is caused by the location and growth on the heart valves of a non-haemolytic streptococcus of which, from serological tests, there appear to be many strains. The valves most frequently affected are the mitral and aortic and the most important predisposing cause is previous rheumatic scarring of these valves. The mechanism of invasion of the valves is not definitely settled, although from the evidence it would appear that the organisms are deposited on the surface from the blood flowing over the valve cusps. Once having gained a foothold the organisms produce a necrosis of the endothelium and adjacent cells and quickly bring about a deposition of platelets, fibrin and leucocytes from the passing blood. In other words the injury of the valve brings about the formation of a thrombus which gradually increases in size. The organisms thrive in the thrombus and are thrown off into the blood stream. In addition, masses of the thrombus itself, large and small, are from time to time dislodged and give rise to the embolic phenomena which more or less characterize the disease.

Once established, the outlook is grave. Libman reports a few recoveries and instances of recurring bacterial endocarditis, but generally the disease progresses—perhaps with slight remissions—slowly to death. The most common cause of death is heart failure, but toxaemia, cerebral embolism and renal insufficiency may terminate the disease.

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The History of Diabetes.

By O. E. A. STEPHENS, 3T4.

The genesis of scientific thinking was the awakening of man to the realization that the first fundamental law of the universe is order; that given certain fixed conditions, certain consequences invariably follow. History indicates that previous to this revelation man was despotically oppressed by fear, mystery and superstition; but as the dawn broke on this long night of bewilderment and ignorance of man, he made crude records of his empirical conceptions and his astonishingly modern ideals. These memorials on earthenware tiles, pottery, rolls of papyrus, reed and other products of archaeological investigations are the annals from which we now study the remote past.

A glimpse at the medical knowledge of ancient Egypt is afforded by the papyrus obtained by George Ebers at Thebes in 1872. This copy of an Egyption medical compilation already old in the time of Moses contains the first description of a case of abnormal polyuria now believed to have been diabetes.

The scientific advancement of European medicine centres in the figure of Hippocrates (460-370 B.C.) who gave to Greek medicine its scientific spirit and its ethical ideals. No future facts that may be revealed about cuneiform or papyric medicine will quite impair the value of the great advance he made in synthetic science. A painstaking search through all his writings, however, fails to reveal any clearly defined description of diabetes. The passages in his works which have been quoted as applying to this disease, seem more to relate to critical urinary discharges. Mention is made there of the excretion of urine being more abundant than the quantity of fluids ingested; but evidently the author only spoke of those critical evacuations which in his opinion terminate diseases.

Nineteen hunderd years ago Aulus Cornelius Celsus wrote a good description of diabetes, including in it some of the chief symptoms, as polyuria and emaciation. He made the claim that patients afflicted with this disease have an excretion of urine exceeding in amount of the fluid taken by mouth. Although this statement might be questioned to-day, it appears to have been accepted by all up until about seventy-five years ago.

Aretaeus, the Cappadocian, (30 A.D.-90 A.D.) comes nearer than any other Greek to the spirit and method of Hippocrates, and as a clinician ranks next to the Father of Medicine in the graphic accuracy and fidelity of his pictures of disease, and is on this account more readily appreciated by modern readers. He is the first to refer to diabetes under its present name. It was he who constructed the word "diabetes," which means "to pass through." The following is an interesting translation from Aretacus' "Of the Causes and Signs of Acute and Chronic Diseases":

"Diabetes is a wasting of the flesh and limbs into urine from a cause similar to dropsy. The patient never ceasing to make water and the discharge is as incessant as a sluice let off. The patient does not survive long for the marasmus is rapid and death speedy. The thirst is ungovernable, the copious potations are more than equalled by the profuse urinary discharge . . . . The epithet diabetes has been assigned from the disorder being something like passing of water by a syphon. . . . . The disease is caused by some of the acute diseases. It is suspected that the pernicious influences of those diseases which attack the bladder and kidneys contain in themselves the cause of this disorder."

Here Aretaeus described the princi-

pal symptoms of diabetes, and called attention to its association at times with acute infectious diseases. He noted all its most striking characteristics except the saccharine state of the urine.

Turning to Hindu medical writings of the sixth century we might borrow the following description of this disease:

"It is a disease of the rich and one brought about by gluttonous overindulgence in rice, flour and sugar . . . . is ushered in by the appearance of morbid secretions about the teeth, ears, nose and eyes . . . . the surface of the skin is shiny as if oil had been applied to it. This is accompanied by thirst and a sweet taste in the mouth . . . . the person is languid, his body becomes fat, and there is a discharge of mucus from the nose and mouth, with dyspeptic symptoms and looseness of the skin. He is always sleepy with cough and difficult breathing. The urine is like the juice of sugar-cane in colour and taste. . . . . it lets fall a hard and small deposit like sand . . . . there are frequent calls to make urine which is discharged in small quantities."

The observers of China and Japan, seventeen hundred and twenty-five years ago, wrote that the urine of diabetics was excessive in amount and that its sweetness attracted dogs; they also noted the occurrence of furunculosis.

Ibna Sina or Avicenna (980-1036) the "Prince of Physicians," was eminently successful in practice as court physician and vizier to different caliphs. His life, however, held too many pleasures and terminated at an early age. In spite of his environment he was a great medical writer, leaving us a remarkable account of diabetes, which includes the essential clinical features of the disease as we know it in modern times. He supported the view of Aretaeus in claiming that diabetes may be primary or secondary to another disease. He recorded that diabetics suffer great thirst, neurasthenia, an inability to work and loss of sex function; also that "the urine leaves a residue like honey." He believed that the liver was involved in the disease; he may have seen enlarged livers in some cases which we would recognize as bronzed diabetes; he also observed that phthisis and carbuncles are frequent complications, and described diabetic gangrene; he concluded that treatment of diabetes was not effective.

Mark Gatenaria has transmitted to us the first example of the disease to be recorded in the annals of the medical science. It is the history of a young girl treated for and cured in 1481, at Milan, of a morbid condition which closely relates to diabetes.

Paracelsus, a chemist, considered diabetes a condition in which there was an increased formation of salt in the blood, "which makes the kidneys thirsty" and causes polyuria. He evaporated a liter of diabetic urine and recovered four ounces of this "salt."

Sylvanus described diabetes as a disease of the blood.

Cardona (1505-1576) gave a detail of treatment and compiled a table in which recorded the quantity of intake of fluid and urinary output in diabetice

Willis (1621-1675- of Oxford University, who classified the cerebral nerves and described the eleventh cranial nerve or "nerve of Willis," made the best qualitative examination of the urine that was possible in his time. Garrison states in his "History of Medicine" that Willis "was the first to notice the characteristic sweetish taste of diabetic urine"; but this is apparently incorrect in the light of Hindu, Japanese, Chinese and Arabian descriptions of the disease.

Regner de Graaf (1641-1673 is especially known for his remarkable work on the structure of the generative organs, having described the follicles in the ovary which have ever since been known by his name. While still a student at Leyden he made an investiga-

tion on pancreatic juice. He made several unsuccessful attempt by various methods to obtain the juice, but he tells us how he finally hit upon the right one. He made use of the quill of the wild duck, which he says "may be got longer and thinner than the quill of any other bird." Into the narrower end of this he inserted a stopper of soft wood, attached to which, and carried through the quill, was a long thread by which the plug could be withdrawn. Having performed tracheatomy on a dog (which he recommends should be fasting) he opened the abdomen, ligatured the duodenum below the pylorus, and below the entrance of the bile and pancreatic ducts, laid open the duodenum, sponged the interior carefully, and then introduced the quill into the mouth of the duct. The broader end was firmly fitted into the neck of a small flask, in the body of which was an orifice for the escape of air, and through which the thread attached to the plug of the quill was drawn. The flask and quill were securely fastened in their place, and the wound in the abdomen, from which the flask hung down, carefully sewn up. The stopper in the quill was then withdrawn by means of the thread, and in a short time the pancreatic juice was observed to drop into the flask. In this way de Graaf obtained from two drams to one ounce of juice in some seven or eight hours. His record of the examination of the qualities of the juice is very meagre. It is interesting to note, however, that this experiment on the pancreas was never, so far as is known, repeated by anyone until Claude Bernard in modern times took it up again.

In 1682, Brunner, the discoverer of the duodenal glands, published a paper entitled "Experimenta Nova Circa Pancreas." His work is the first to reveal that the pancreas is necessary for the complete utilization of carbohydrates in the animal body. In one of his experiments he removed the spleen, and when the animal had recuperated somewhat, he removed the pancreas also, "it was especially to be seen that the animal made water frequently, and that he was very thirsty, drinking largely of water in proportion to the discharge of urine." An interesting translation is given in Foster's "History of Physiology" of another experiment in which Brunner depancreatized a dog. Brunner remarks. "I had bought the animal from a butcher, and after the operation it was also hungry. It was continually going to its old master's shop and stealing pieces of meat. Indeed it carried on the game to such an extent that the dealer came to me and demanded that it should be killed. This, however, I put off doing since I wanted to enjoy for some time longer such a pleasant experience as the animal's condition afforded me."

The summation of Brunner's conclusions drawn from his observations of animals after extirpation of the pancreas, was that *their health remained unimpaired and that the pancreatic juice did not play an important role in the process of digestion.* The monds of physiologists therefore reverted to the older view that the stomach was the chief seat of digestion, and for more than a century and a half no one thought it worth while to seek for any function of the pancreas.

In 1776, Matthew Dobson in his "Experiments and Observations on the Urine in a Diabetes," describes a series of meticulously performed and recorded experiments. He saye that the kidney secretions "had very little of the nature of sensible qualities of urine, but contained a substance which readily passed through the vinous, acetous and putrefactive fermentations."

In 1788, Thomas Cawley published, in the London Medical Journal, the first case of diabetes mellitus accompanied by lesions of the pancreas. According to his report the process developed in about six months and the autopsy revealed a pancreas stuffed with calculi,

while the right end of the gland was hard and waxy.

The period of empiric treatment began about 1796, when Rollo, an Englishman, began treating diabetes by restricted dieting. His idea was to reduce the activity of the stomach as he thought that diabetes was caused by corrupted gastric juice.

Chevreul (1815) showed that sugar elimination in diabetic urine was identical with grape sugar. This had the fortunate result in narrowing the number of kinds of diabetes from seven to two, namely, diabetes mellitus and insipidus.

Mailhe discovered that saliva cantained diastase, and about two weeks later Bouchardat found a similar substance in the pancreatic juice.

Bouchardat (1806-1886) laid down the most rational treatment for the disease up to his time. He insisted on strict diet, substituting fresh fats for carbohydrates, eliminating milk because of its lactose, including alcohol as a food and administered alkalies. He noted that during the siege of Paris, when food was scarce, glycosuria disappeared in diabetes, just as it did in Germany during the Great War.

With Bouchardat the modern viewpoint of diabetes begins. More has been learned of diabetes during the past sixty years than in the previous eighteen hundred and fifty years.

Ambrosiana, an Italian chemist, showed the presence of a fermentable sugar in diabetic blood.

In 1848, Herman von Fehling developed his well-known sugar test.

The next important advance was made by Claude Bernard, (1813-1877) the great master of modern experimental physiology, who succeeded in isolating glycogen. In his thesis for the M. D., "On the Gastric Juice and its Role in Digestion," we find the nucleus of one of his great discoveries. He observed that cane-sugar injected into the blood is excreted in the urine, but that such is not the case if it be previously acted upon by the gastric juice. He showed experimentally that the hepatic vein contained more sugar than the portal vein and that if the animal be given food containing neither starch nor sugar or if it be starved, sugar is still found in the hepatic vein. He washed the veins of the liver until they were free from sugar, and after some time tested again and found sugar present in the hepatic vein. He concluded that besides forming bile, the liver makes sugar which it pours into the blood. Bernard isolated glycogen from the liver by the potash-alcohol process in 1857. While studying the influence of nerves on glands, it occurred to Bernard that the vagus might be concerned in the secretion of glycogen in liver cells. On puncturing the floor of the fourth ventricle to injure the origin of the vagus he produced "artificial glycosuria" or "experimental diabetes."

Starting from the inexact fact that the sugar in the blood of a diabetic is without action on polarized light, Cantani put forward the idea that it was on isomer of glucose, whose production brought about drastic chemical changes in the pancreatic cells.

In the "Medio-Chirurgical Transactions," 1833, Bright called attention to the presence of fat in the feces of a diabetic—a symptom to which little importance had as yet been attributed.

Naunyn (1839) devoted nearly his whole life to the study of metabolism in diabetes and in disease of the pancreas. One of his most important works was his monograph on diabetes. He introduced the concept of diabetic coma as a fatal acidosis. The principles of his dietetic treatment are applicable to-day.

Paul Langerhans, an anatomist, in his "Berlin Dissertation, 1869," described the peculiar collections of cells in the pancreas, the Isles of Langerhans, which were later to be revealed as a very pertinent factor in the causation of diabetes.

Coming to 1878, we find that Lancer-

eaux enunciated the relationship existing between lesions of the pancreas and the production of glycosuria; he then built up his theory of pancreatic diabetes. Enthusiasm spread, many observers maintaining that most cases of diabetes mellitus were due to pancreatic lesions; but experimental proof of Lancereaux's theory was wanting; therefore, great was the joy when in 1889 von Mering and Minkowski were successful in producing glycosuria, hyperglycemia, marked emaciation and finally death in animals following extirpation of the pancreas. To insure best results, they stressed the importance of dissecting out every trace of the gland and of having aseptic conditions in the operation. They did not say in what way pancreatic ablation caused diabetes, but their work strengthened the opinion of the part played by the pancreas in the production of the disease. Their work was a forerunner of many interesting experiments, in some of which only parts of the gland were removed resulting in various kinds of diabetes. In complete removal an intense diabetes ensued, and partial extirpation resulted in a mild form of the disease; lastly in depancreatised dogs, with a subcutaneous graft of a bit of the gland, diabetes arose only when the graft was removed.

Lemoine considered a lesion of the pancreatic acini as being included in the etiology of the disease.

Von Mering and Minkowski concluded in 1892 that diabetes following ablation of the pancreas was due to interference with an unknown function of the pancreas.

Hauseman claimed the lesion of the parenchyma as exclusively diabetogenous, because, he said, he found the island of Langerhans normal in autopsies on diabetics. Others regarded insular secretion as the anatomical cause of the disease.

Lepine, in 1894, put forth the theory that the pancreas secretes a glycolytic ferment which destroys the sugar.

Frederick Pavy, a colleague of Bernard, inferred that the excess of sugar which Bernard obtained from the liver was entirely due to postmortem changes in that organ. By many ingenious arguments, based largely on his own work, he showed that glycogen is not changed into sugar by the liver during life, that oxygen does not destroy the sugar in the blood, and that glycogen itself occurs in the blood. However, the last experiment that Pavy performed indicated that more than 150 grams of dextrose per hour could be injected into the blood without appearing in the urine, thus exploding the principal argument upon which he based his theory. He was undoubtedly right, however, in holding that too much stress had been laid upon the liver as a sugar producer.

In 1901, Opie concluded from observation of a number of cases that "diabetes mellitus when the result of a lesion of the pancreas is caused by destruction of the islands of Langerhans and occurs only when these bodies are in part or wholly destroyed." He also believed that the acini of the pancreas were not involved. He says, "Where diabetes was absent the isands persisted unaltered though the secreting parenchyma was in large part destroyed . . . in the present case, however, diabetes followed a lesion affecting only the islands of Langerhans.

Zuelzer, a German investigator, was probably the most successful of earlier workers in demonstrating the existence of an internal secretion of the pancreas, the presence of which removed the symptoms of diabetes. In 1908 he succeeded in preparing from the pressed out juice of adult ox pancreas, by means of alcohol, an extract which, when injected subcutaneously into animals, could remove the hyperglycemia and glycosuria produced by administering epinephrin. He administered the extract to eight diabetic patients and in five obtained decidedly favourable results. The sugar nearly disappeared

from the urine, acetone bodies became much less; the patients improved generally and it looked as if the antidiabetic hormone had at least been discovered. The extracts, however, produced toxic effects which overshadowed any beneficial action and the research was abandoned. There can be no doubt that Zuelzer very nearly isolated insulin in 1908.

Rennie and Fraser also came very near to capturing the elusive hormone but also missed it because they were frightened by toxic symptoms, the cause, for which, they could not understand.

The repeated failures to prepare pancreatic extracts that could relieve symptoms of diabetes and be safe for administration to man seemed to discourage any further attempt in this direction and the problem of the extraction of the antidiabetic principle from the pancreas became the problem exclusively of the physiologists and biochemists among whom were Knowlton, Starling, Evans, Scott, Kleiner and Murlin.

Guelpa of Paris, 1910, maintained that diabetes was due to intestinal toxemia and recommended periodical fasting as a treatment. He showed that by abstinence of food and thorough evacuation of the intestines with a saline laxativity, sugar disappears from the urine in most cases within three days. Guelpa's work was thought by his contemporaries, as being of great significance, as they considered that the facts brought forward by him completely upset established ideas concerning the pathogeny of diabetes.

On October 30th, 1920, a London, Ontario, practitioner, Dr. F. G. Banting, was attracted by an article by Moses Baron, in which he pointed out the similarity between the degenerative changes in the acinus cells of the pancreas following experimental ligation of the duct, and the changes following blockage of the duct with gall-stones. Dr. Banting says, "After reading the article by Baron, I was unable to sleep. There seemed to be, in some vague way, a relation between the islet cells of the pancreas and clinical diabetes. There seemed also to be a means of attacking the problem of extracting the island cells. It was not until 2 o'clock in the morning that I was able to crystallize the idea into a form that would lend itsef to experimentation. At this hour, I arose and wrote in my note-book the following words: "*Ligate pancreatic ducts of dogs. Wait six to eight weeks for degeneration. Remove the residue and extract.*"

The story of the isolation of the antidiabetic hormone by Drs. Banting and Best beginning April 4th, 1921, is familiar to us all and need not be repeated here.

The history of diabetes does not end with the discovery of insulin, for insulin is not a cure for diabetes; it is a treatment; but as a treatment it enables the emaciated, pessimistic, melancholy diabetic to regain his health and natural composure, and to face the economic burdens of life optimistically, cheerfully and with renewed energy.

The recent advances in research concerning diabetes depend to a very great degree on the work done by the men who have gone before; future accomplishments will be indebted in large part to the work of the investigators of to-day. Thus also does modern medicine of this great age stand on the shoulders of the ages which have gone before. Her value is in large part a debt to her precursors; her vision is always directed to the ever receding horizon, and her ultimate goal, co-ordinate with the progress of all sister sciences, is the prediction and control of phenomena, the prevention as inclusive of the cure, of disease. She has no fairer ideal than that expressed in the beautiful phraseology of Minot:

"We have enthroned science in the imagination, but we have crowned her with modesty, for she is at once the

reality of human power and the personification of human fallibility."

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The Aschheim—Zondek Test for Pregnancy.

By G. L. MORGAN SMITH, B.A.

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In recent years the biological tests for chemical compounds have been greatly improved, enabling one in many cases to detect very minute amounts of a substance. When Smith and Engle (1) in America and Aschheim and Zondek (2) in Germany, observed the stimulating effects of extracts of the anterior pituitary gland on the ovaries of rodents, the path was opened for the detection of a material, physiologically the same as the anterior pituitary hormone, that is excreted in the urine of pregnant women. It is to the German workers (3) that we owe this discovery.

When suitably prepared extracts of either the anterior pituitary gland or the placenta, or urine of pregnant women are injected into immature mice, the ovaries are stimulated to sudden growth. The Graafian follicles ripen, and haemorrhage occurs often into the unruptured follicle, forming the corpue haemorrhagicum, or blood spot. This latter is replaced by luteal tissue. At the same time the ovary elaborates a hormone, oestrin, which ensues hypertropny of the genital tract. The picture presented by a mouse so treated is in marked contrast to that displayed by its litter mate control which has small ovaries and a thread-like uterus. It is this marked effect on the immature ovary that is used as a test for the anterior pituitary-like hormone.

Since the urine of pregnant women contains a substance which causes the above changes, this fact has been used as a test for pregnancy. It has found that a positive reaction is given from a period within three weeks of conception to seven or eight days past partum. Ectopic pregnancies, hydatidiform mole, and chorionepithelioma also give positive reaction showing that active trophoblast, rather than the presence of the foetus determines the reaction.

Cases which may be confused with pregnancy but which give a negative result to this test may be summarized as follows:

Amenorrhoea, due to various causes.
Oligomenorrhoea.
Tumours of the genital tract.
Dead foetus.
Menopause.
Pelvic abscesses.

Technique.

Five immature mice, 3-5 weeks old, weighing 6-8 grams are used. These are injected subcutaneously with 2 c.c. of an early morning specimen of urine, divided in six equal doses over a period of three days. On the fourth day one of the mice is killed. If the reaction is positive the remainder of the mice are killed and the result of the test known on the fourth day. If the reaction in the first mouse is negative, the remaining four are left until the following day in case the development may be completed in the next 24 hours. On autopsy a positive test is one in which the ovaries exhibit one or more blood-spots or corpora lutea. Absence of these structures constitutes a negative test. These changes are quite visible microscopically, and may be confirmed by microscopic observations.

It is very convenient that the urine need not be treated in any way. In cases where bacterial action is possible, further growth will be stopped by the addition of one or two drops of tricresol. This particularly applies to specimens sent by mail. Occasionally a sample is encountered which kills the mice. Often such urines may be rendered less toxic by shaking with ether and discarding the ether fraction. The last traces of ether are removed in vacuo at room temperature.

The Rabbit Test.

A modification of the Aschheim-Zondek reaction is the rabbit test devised by Friedman (3). It has the advantage over the mouse test of requiring only 2-4 hours for its completion. 5 c.c. of urine is injected into the ear vein of a three-months' old habbit, and the same changes sought in the ovary that occur in the mouse. In 200 cases observed by Schneider (5) the rabbit test gives the same accuracy as the Aschheim-Zdndek test.

The greater expense of the rabbit test, together with the difficulty of obtaining rabbits of the right age render the Aschheim-Zondek test more feasible, except in cases where rapid diagnosis is desired.

During pregnancy the urine contains at least 3 hormones. Prolan A and Prolan B (Rho 1 and Rho 2) are the two that act on the ovary of the immature mouse, the first causing growth and ripening of the Graafian follicle, the second lutealization. Oestrin is also present, and is tested for by its effect in causing oestrus or heat in the ovariectomized rodent. This reaction has been used as a test for pregnancy, but may introduce an error due to the fact that certain ovarian disorders may cause a positive reaction. Moreover the evidence seems to show that oestrin is not present in such large amounts in early pregnancy as the anterior pituitary-like hormone.

The reason for the presence in the prine of such large amounts of these various hormones during pregnancy is hard to explain. This is a fascinating problem which can only be solved by further discoveries in the endocrine field.

In the literature one frequently comes across the term "placental hormone." This is based on the supposition that the anterior pituitary-like hormone is elaborated in the placenta. The weight of the evidence seems to contradict that view specially since hypertrophy of the anterior pituitary during pregnancy is observed and since the Aschheim-Zondek test is positive in such a short time after implantation when the trophoblast tisssue must be very small.

The report of tests on over 4,800 cases may be found in the literature. The percentage accuracy is approximately 98.2 per cent. In arriving at this figure the work of Louria and Rosenzweig (6) who used mice weighing 10 grams or over is omitted, since this introduced an error due to the occurrence of normal, spontaneous sexual maturity. The work of Mazer and Hoffman, who discredit the test, is also omitted because their results have a large error, at variance with the majority of workers. This may be due to the fact that they used only two mice instead of five for each specimen of urine.

The results obtained in this department and in The School of Hygiene, on 140 cases are in accordance with those found in other centres. Particularly interesting are one case of hydatidiform mole and one of ectopic pregnancy which gave positive tests. Among the cases giving negative results were those subsequently diagnosed as amenorrhoaea due to various causes, adeno-carcinoma of the ovary, missed abortion, and fibroids of the uterus.

From the work that has been done on the Aschheim-Zondek test for pregnancy, it would seem to be a very useful aid to the clinician. At present it is not generally available, but the technique is of such nature that it could be readily and cheapily carried out in hospital or public health laboratories. The time may come when this test will be as readily available for the practising physician, as are many chemical and bacteriological tests at the present time.

The research work of this paper was carried out with Dr. E. W. Henry in the Department of Physiological Hygiene, under the direction of Professor C. H. Best, for whose kindly advice and criticism we are greatly indebted.

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BOOK NOTES

J. George Adami—A Memoir.

By MARIE ADAMI.

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The name Adami is known to most of us, but one wonders how seldom it is known but as a text book reference. We know that he was a pathologist; that he was an authority is certain from the frequent occurrence of his name; but of the great spirit of the man, of those years at Montreal, his devotion to the task of building from the ground a department of pathology which was the forerunner of the best we have to-day—how much do we know? It was a monumental task, and in truth, he gave his life to it. When he left it he had accomplished all that one man in one age could have done, and left behind him a memorial which should little need the aid of a memoir to embellish its greatness. But we forget. And when those have gone who knew him and labored with him, and loved him, we will still remember his work at least in one aspect, but of the man himself we will know but little. That is why this able and graceful tribute recommends itself to every student of medicine.

Scattered throughout the Medical Schools of Canada and the United States are the remaining members of that band of eager, ambitious young men whom Adami gathered about him, and to whom, with infinite care and devotion he taught those principles which now guide the best teaching of pathological science throughout the continent. He encouraged them along the lines of original research. Of this Professor Klotz in his "Recollections of Montreal," says: "The general feature surrounding these laboratories was a sense of freedom to pursue one's work as one felt inclined, without the urge of outside influence, without the demand for gaining preconceived results, without the interference aroused by over enthusiasm, and with the maintenance of a sincere cordiality between each and every one who was housed under this common roof." To them, above all, he taught the paramount importanace of the intimate co-relation of laboratory science with the clinic, the emancipation of the autopsy room from the "dead-house." By example he taught them that devotion to duty which so characterized his own life.

In addition to the main biographical work by Marie Adami, there are six added contributions by men of eminence in this field of work. Professor A. G. Nichols, of Dalhousie, Professor C. F. Martin, of McGill, Dr. Maude Abbot, of McGill, Professor C. S. Worthin, of Michigan, Dr. Ernest Barker, of Cambridge, and Professor Oskar Klotz, of Toronto, from whose contribution we quoted above.

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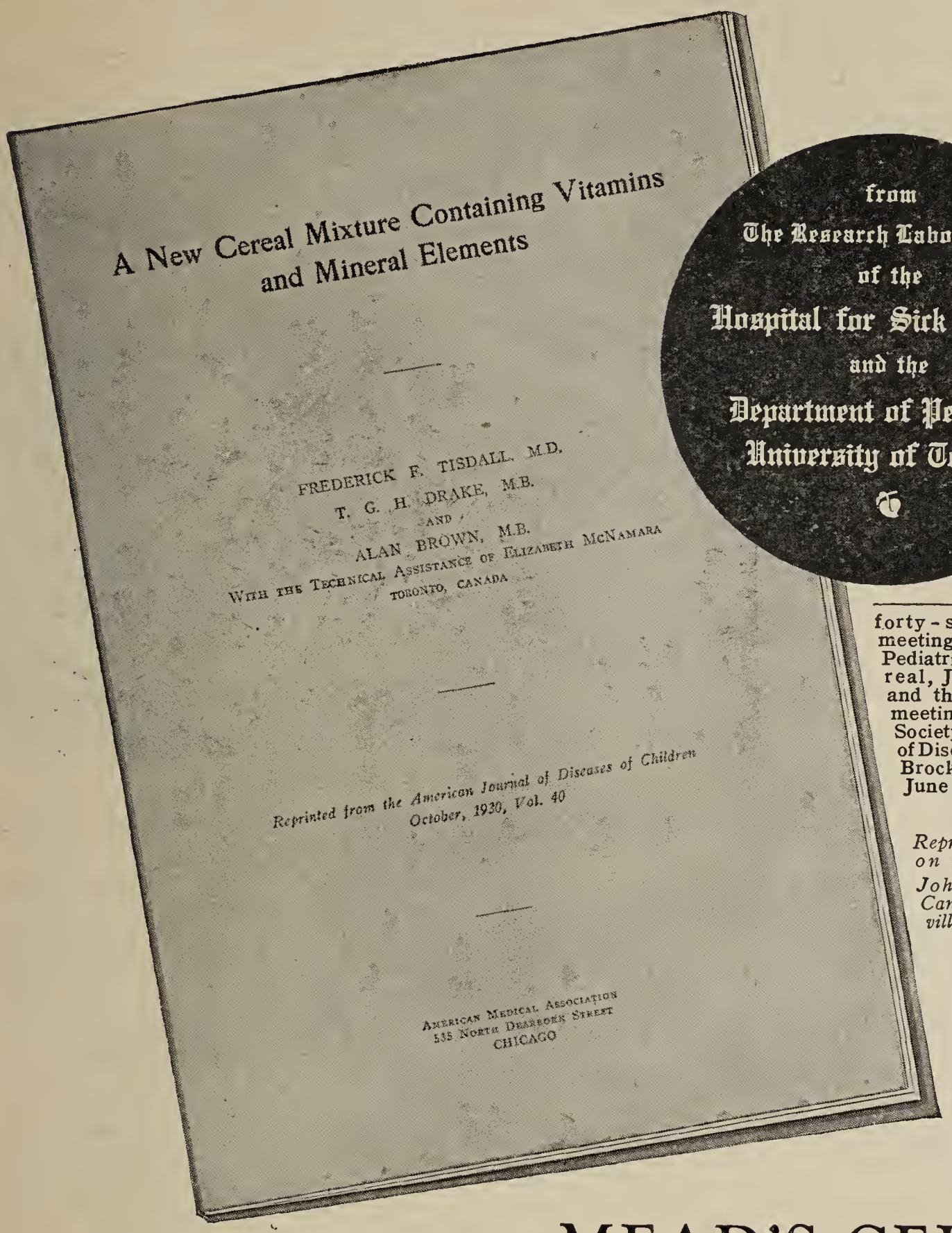
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*Journal of American Medical Association, Aug. 27, 1927, page 694.

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